STUDY OF CARDIOVASCULAR MANIFESTATIONS IN ANKYLOSING SPONDYLITIS

conducted at

COIMBTAORE MEDICAL COLLEGE

Submitted in partial fulfillment of the requirements

for the award of the degree

M.D. GENERAL MEDICINE

BRANCH -1

to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY CHENNAI

APRIL 2016

CERTIFICATE

Certified that this is the bonafide dissertation done by ***Dr.BARATHI.L****. and submitted in partial fulfillment of the requirements for the Degree of* ***M.D.,General Medicine,*** *Branch I of* ***The Tamilnadu DR. M.G.R.Medical University Chennai.***

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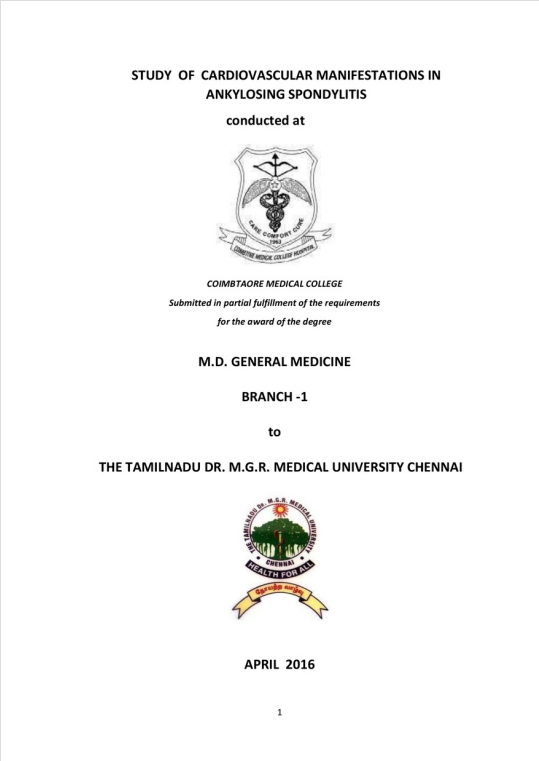

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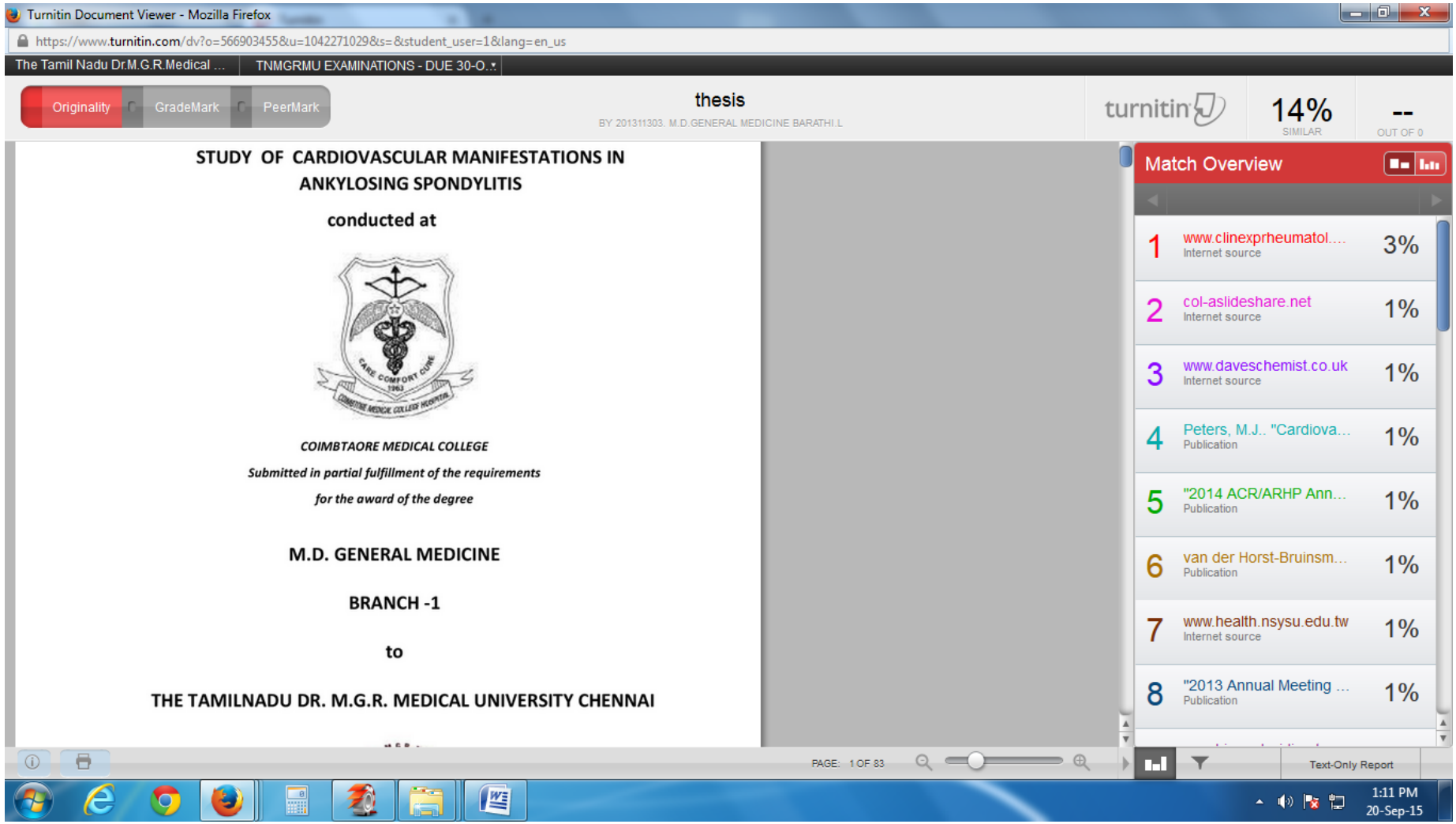
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DECLARATION

I solemnly declare that this dissertation entitled **" STUDY OF CARDIOVASCULAR MANIFESTATIONS IN ANKYLOSING SPONDYLITIS"** is a bonafide and genuine research work carried out by me at Coimbatore Medical College and Hospital from July 2014 to July 2015, during the academic year 2013-2016 under the guidance and supervision of **Dr. KUMAR NATARAJAN MD.,** Head Of the Department, Department of Medicine, Coimbatore Medical College Hospital, Coimbatore.

This dissertation is submitted to the Tamil Nadu Dr.M.G.R. Medical University, towards the partial fulfilment of requirement for the award of M.D.Degree in General Medicine (Branch-I).

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ACKNOWLEDGEMENT

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Dr. BARATHI.L

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LIST OF ABBREVIATIONS

AS	:	Ankylosing Spondylitis
ASAS	:	Assessment of Spondyloarthritis International Society
TNF	:	Tumour Necrosis Factor
IL	:	Interleukin
CD	:	Cluster of Differentiation
HRCT	:	High Resolution Computed Tomography
ESSG	:	European Spondyloarthritis Study Group
CT	:	Computed Tomography
CXR	:	Chest X Ray
ESR	:	Erythrocyte Sedimentation Rate
CRP	:	C Reactive Protein
DIP	:	Distal Interphalangeal joint
PIP	:	Proximal Interphalangeal Joint
ECG	:	Electrocardiogram
ECHO	:	Echocardiogram
RVol	:	Regurgitant Volume
RF	:	Regurgitant Fraction
ERO	:	Effective Regurgitant Orifice
LA	:	Left Atrium
IAS	:	Inter Atrial Septum
IVS	:	Inter Ventricular Septum

INTRODUCTION

INTRODUCTION

Ankylosing spondylitis is a chronic inflammatory disorder primarily affecting the sacroiliac joints and vertebral column, often manifesting in young males than in females in the ratio of 3:1 in the second or third decade.

Even though ankylosing spondylitis is principally a disease of axial and peripheral joints, extraarticular manifestations of the disease are also common, affecting Cardiac, ophthalmic, pulmonary, renal and neurological systems.

Ankylosing spondylitis has a worldwide prevalence of 0.1 to 1.4%. The prevalence of rheumatoid arthritis among Indian population is found to be 0.85%. According to Yang et al, the prevalence of cardiac manifestations in ankylosing spondylitis patients were found to be 10% to 30%

Bulkley and Roberts were one of the first to put forward pathophysiologic description of valvular heart diseases in ankylosing spondylitis, when they studied autopsy findings in eight patients with ankylosing spondylitis. They demonstrated aortic root dilatation, with a cellular inflammatory process with fibroplast overactivity along with tissue thickening involving the aortic cusps, aortic annulus, conduction system leading to aortic regurgitation and conduction abnormalities in patients with ankylosing spondylitis.

Thereafter a lot of research works were carried out regarding the cardiac manifestations in patients with ankylosing spondylitis and found that aortic regurgitation, aortic root dilatation and conduction disturbances were the most

common abnormalities. The other associations were pericarditis, myocarditis, left ventricular diastolic dysfunction, mitral regurgitation.

The cardiac manifestations in ankylosing spondylitis can be symptomatic or asymptomatic. Hence the patients with ankylosing spondylitis should be screened for cardiac abnormalities by electrocardiography and echocardiography.

O'Neill, T. W.et al,[34](1992) found out that 29% of patients with ankylosing spondylitis were associated with cardiac abnormalities.The abnormalities were found in patients with ten or more than ten years duration. Cardiac abnormalities associated were aortic incompetence, pericardial effusion and conduction disturbances.

Park et al, depending on the disease duration, found out the early valvular involvement in young males with ankylosing Spondylitis using transoesophageal echocardiography. They measured the aortic valve thickness, mitral valve thickness, aortic root diameter.

Many studies were carried out in relation to cardiovascular manifestations in ankylosing spondylitis and had found that the association of cardiac manifestations increased with increased duration of ankylosing spondylitis , increase in the age of the patient.

AIMS & OBJECTIVES

AIMS AND OBJECTIVES:

AIM:

To find the prevalence of cardiovascular manifestations in patients suffering from Ankylosing Spondylitis.

OBJECTIVES:

- To observe the cardiovascular manifestations in patients with Ankylosing Spondylitis by chest X Ray, electrocardiography and echocardiogram compared with the controls.
- To find out the relation between cardiac lesions with the age, sex of the patient, clinical parameters, Grading by X Ray and duration of Ankylosing Spondylitis.

REVIEW OF LITERATURE

HISTORICAL ASPECTS:

Anatomical descriptions of two skeletons typical of ankylosing spondylitis was given by Realdo de Colombo in 1559. Later several descriptions of ankylosing spondylitis came in the nineteenth century. Sir Benjamin Brodie in 1850, described ankylosing spondylitis in a man whose disease started at 27 years of his age and became completely rigid after 6 years with a 'hoop-like' deformity of the spine and associated with inflammation of the eyes. This was the first reported case of uveitis in a patient with ankylosing spondylitis.

Charles Fagge , a clinician at Guy's Hospital in 1877 described cardiac, pulmonary manifestations in a man of 34 years. Bechterew, a neurologist who in 19^{th} century described neurological manifestations in three patients, a mother and daughter and a man who had incurred trauma to his back in the past. With the clinical data he assumed a chronic process of the vertebrae leading to ankylosis which probably leads to a diffuse chronic inflammation of the epidural connective tissue with pressure on the nerve roots, that sufficiently explains the rigidity or stiffness of the vertebral column, as well as the sensory symptoms of the spinal nerve roots with weakness of the muscles of the neck, back and upper extremities. Bechterew favoured a genetic predisposition for ankylosing spondylitis since he observed the disease in both mother and the daughter.

Berlin Adolph Strűmpell in 1897, described two patients with complete ankylosis of the spine and of both hip joints. He emphasised lumbar lordosis in a rigid spine as a prominent feature and published photographs of such patients. Strűmpell labelled the disease in more descriptive terms as 'chronic inflammation of the large joints and vertebral column'.

Pierre Marie in 1926 gave the detailed and characteristic clinical description of ankylosing spondylitis and coined the word 'spondylose rhizomélique'. He gave detailed descriptions of six male patients. He worked as an assistant to Jean Marie Charcot at the Salpêtrière Hospital before becoming Professor of Neurology. Léri, Marie's assistant, described the full pathological characteristics of ankylosing spondylitis after he had carried out autopsies on two of Pierre Marie's patients. His conclusions anticipated modern developments.

Ankylosing spondylitis, hence named after the major contributors of the description of the disease as Bechterews disease or Marie – Strumpell disease Association of ankylosing spondylitis with aortic incompetence was described by Charles W Hufnagel in 1956, when 100 patients with prosthetic aortic valve were reviewed. Among them he found five patients had Ankylosing spondylitis.

DEFINITION OF ANKYLOSING SPONDYLITIS:

Ankylosing spondylitis (AS) is a chronic inflammatory disorder predominantly affecting the sacroiliac joints and vertebral column which often

manifests in young males than in females in the second or third decade. Extraarticular manifestations of the Ankylosing spondylitis includes arthritis of the peripheral joints, enthesitis, anterior uveitis, prostatitis, cardiac and pulmonary manifestations[1,2]

ETIOLOGY:

Etiology of Ankylosing spondylitis is multifactorial, based on endogenous and exogenous causes. Endogenous factors involve the genetic component with increased prevalence of the disease in the population with HLA-B27 gene located in the chromosome 6 with increased familial recurrence[3]

Other genes that encode for the production of pro-inflammatory cytokines, like interleukin1 (chromosome 2q14), Interleukin 1 alfa and beta polymorphisms, as well as the polymorphisms of its functional antagonist the interleukin 1 receptor antagonist gene. CARD 15, related to Crohn's disease[4] and the gene encoding for the human Transforming Growth Factor B1 (TGFB1) , a regulator of osteoblast proliferation also plays a role.[5] Exogenous factors involve certain bacterial infections like salmonella and Chlamydia.

PATHOLOGY OF ANKYLOSING SPONDYLITIS

The disease involves both axial and peripheral skeleton, though the axial skeleton gets involved at the earliest. Inflammation in the fibrocartilagenous enthesis, the region where a tendon, ligament, or a joint capsule attaches to bone, is a characteristic lesion in AS and other spondyloarthritides, both at

axial and peripheral sites. This enthesitis is associated with prominent edema of the adjacent bone marrow and is often characterized by erosive lesions that eventually undergo ossification.

Sacroiliitis is often the earliest manifestation of AS. Synovitis,the earliest change will be followed by pannus and subchondral granulation tissue formation. This is followed by fibrocartilage regeneration of eroded joint margins and then by ossification.

Spinal specimens studied have shown inflammatory granulation tissue at the junction of annulus fibrosus with the vertebral bone. The outer annular fibres are eroded and eventually replaced by bone, forming the beginning of a syndesmophyte, which then grows by continued enchondral ossification eventually bridging the adjacent vertebral bodies thus giving rise to a "Bamboo Spine". Erosion of joint cartilage by pannus formation is often followed by bony ankylosis. Bone mineral density is diminished in the spine and proximal femur early in the course of the disease.

The features of peripheral arthritis in AS and other forms of SpA are similar, and distinct from those of rheumatoid arthritis. Synovitis is associated with marked vascularity, evident as tortuous macrovascularity seen during arthroscopy. Lining layer hyperplasia, lymphoid infiltration and pannus formation are also found. Proliferation of subchondral granulation tissue leading to central cartilaginous erosions are common.

Subclinical intestinal inflammation in the colon and distal ileum has been found in a majority of patients with AS and other forms of SpA. Acute lesions resemble bacterial enteritis with largely intact architecture and neutrophilic infiltration in the lamina propria. The chronic lesions are associated with distortion of crypts and villi, aphthoid ulceration and mononuclear cell infiltration in the lamina propria.

PATHOGENESIS OF ANKYLOSING SPONDYLOSIS

The pathogenesis is immune-imediated with evidences suggesting more of an autoinflammatory process rather than antigen-specific autoimmunity. TNF-α, a cytokine plays a central role in the immunopathogenesis of AS as evidenced by the therapeutic response to anti-TNF-α drugs. More recent evidence stongly implicates the IL-23 / IL-17 cytokine pathway in AS pathogenesis. The genes implicated are IL-23, IL12B, and CARD9. Serum levels of IL-23 and IL-17 are elevated in AS patients. IL-17 is largely produced by mast cells and to a lesser extent by neutrophils in the setting of peripheral arthritis in AS where as neutrophils are the major IL-17 producing cells in apophyseal joints. High levels of circulating γδ T cells expressing IL-23 receptors and producing IL-17 have been found in AS patients.

CD4+ and CD8+ T cell and macrophage infiltration with high levels of TNF-α are found in the inflammed sacroiliac joints, early in the disease. More advanced lesions show abundant levels of TGF-β. Peripheral synovitis show abundant neutrophils, and macrophages expressing CD68 and CD163, CD4+

and CD8+ T cells and B cells. Intercellular Adhesion Molecule 1 (ICAM-1), Vascular Cell Adhesion Molecule (VCAM-1) , Matrix Metallo Proteinase (MMP-3) , and Myeloid Related Proteins (MRP 8 and 14) are also implicated in the pathogenesis.

Overlapping features with reactive arthritis and IBD and involvement of IL-23/IL-27 pathway suggest that enteric bacteria may play a role, and microdamage from mechanical stress at enthesial sites has also been implicated.

Though the association of HLA-B27 with AS and its direct role in AS pathogenesis has been firmly established, its exact role at the molecular level remains unresolved. Several theories have been postulated as possible mechanisms, with or without the involvement of antigen presentation. Also, a role for natural killer cells has also been suggested possibly through interactions between B27 heavy chain homodimers and killer cell immunoglobulin like receptors inducing pro-inflammatory leukocytes in the disease.

Recent evidences point out a strong association between ERAP 1 (Endoplasmic Reticulum Amino Peptidase 1) and HLA-B27 positive ankylosing spondylitis. ERAP 1 in these patients have lower aminopeptidase activity than the normal individuals and this combined with HLA-B27 heavy chain has higher tendency to misfold and pay way for a strong pro-inflammatory milieu.

New bone formation in AS is largely due to enchondral bone formation and whether this is secondary to inflammation or not is a matter of debate. Evidences point out to lack of regulation in Wnt signal transduction pathways which controls the osteophyte formation with the help of inhibitors like DKK 1(Dickkopf Related Protein 1) and Sclerostin. Anti-TNF-α therapy suppresses the ongoing inflammation whereas it fails to suppress new bone formation suggesting an independent mechanism for new bone formation. However, recent evidences based on MRI studies reveals that prolonged inflammation at enthesial sites leads to fatty tissue metaplasia and this subsequently becomes the predominant site for syndesmophyte formation. However, recent evidences suggest that continued Anti-TNF-α therapy may decrease the rate of this syndesmophyte formation.

CLINICAL FEATURES:

Average age of onset of the disease is about 28 years but can also occur in children, called as juvenile onset AS, dominated by peripheral arthritis.Onset after the age of 45 years is very uncommon. The complaints in AS are often gradual with mean delay of 8 years from the onset of first symptoms to the onset of diagnosis. The disease occurs more common in males with a male to female ratio of approximately 3:1. The age of onset is slightly higher in females[6]. In men the disease manifestations are most commonly located in the spine and pelvis, whereas in women it commonly involves the peripheral joints and pelvis[7]. The disease tends to be more severe in men with a higher incidence of uveitis.

Spinal manifestations:

The spinal involvement results in chronic inflammatory back ache with morning stiffness caused by inflammation of the sacroiliac (SI) joints and vertebral column. Morning stiffness improves with exercise and lasts atleast for one hour. Sacroiliitis,the most important characteristic of AS can be detected by a conventional radiograph of the pelvis showing blurring of the distal part of the SI-joints, progressing to joint space narrowing and finally sclerosis of the joints. At initial stage Magnetic Resonance Imaging(MRI) is more sensitive[8]. Involvement of the cervical and costovertebral joints causes pain in the cervical and thoracic spine especially with chest expansion.

Spinal inflammation coincides with the formation of syndesmophytes and squarring of the vertebrae, causing classical bamboo spine which leads to spinal ankylosis with limitation of chest expansion and neck movements and flattening of the lumbar spine and thoracic kyphosis resulting in a stooped forward posture.

Atlanto-axial subluxation might occur due to erosions of the transverse ligaments that leads to neurological complications. Osteoporosis occurs in patients with syndesmophytes peripheral joint involvement which leads to fractures even after a minor trauma. Another spinal complication is non-infectious spondylodiscitis which occurs in approximately 8% of the AS patients, predominantly at the thoracic and lumbar levels.

Figure 1: Bilateral sacroiliitis

Figure 2: Spinal inflammation with syndesmophytes

The disease activity is measured by BASDAI (Bath Ankylosing Spondylitis Disease Activity Index). It consists of a scale from 1 to 10, with respect to the increase in the severity of the problems. It consists of 6 questions with 5 major problems.

- Incresae in tiredness
- Pain over the spine
- Swelling or pain over the joint

- Extra articular tenderness
- Duration of morning stiffness and
- Severity of morning stiffness.

To give equal weighting to each symptom, the mean of two scores relating to morning stiffness is taken. The resulting 0 to 50 score is divided by 5 to give a final 0 – 10 BASDAI score. Scores of 4 or greater suggest suboptimal control of disease and those are usually good candidates for either a change in their medical therapy or for enrollment in clinical trials evaluating new drug therapies directed at Ankylosing Spondylitis. BASDAI is a quick, simple and reliable index for treatment outcome.

EXTRASPINAL MANIFESTATIONS:

Arthritis:

Peripheral arthritis usually occurs in one third of the patients, especially in the knees, shoulders and hips[9]. Hip involvement is common in the juvenile-onset and is usually bilateral which occurs mainly in the first ten years of the disease.This leads to flexion contracture and destruction of the affected hip joint that ultimately requires joint replacement.Shoulder joints are also usually involved. Knees, wrists, elbows and feet are usually involved in an asymmetrical pattern. Radiographic features show bony ankylosis.

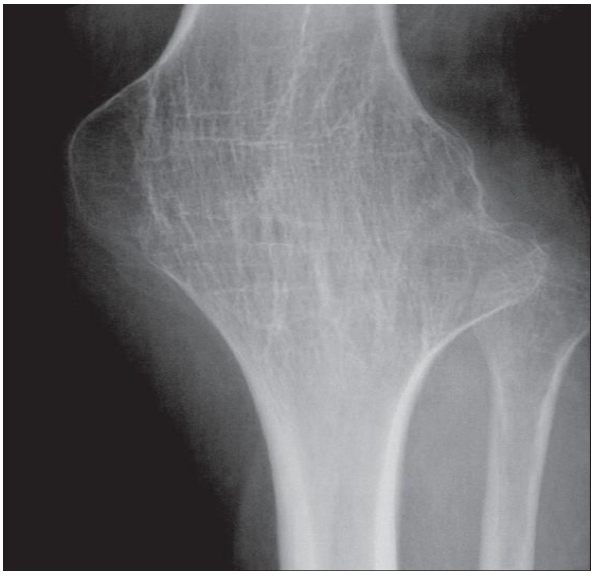


Figure 3: Arthritis of knee joint in AS

Enthesitis:

Enthesitis, an extra-articular bony tenderness caused by local inflammation causes pain. Many sites can be involved like costosternal junctions, spinous processes, iliac crests, greater trochanters, ischial tuberosities, tibial tubercles or tendons insertions like the Achilles tendons[10].

Figure 4: Heel enthesitis in AS

Ocular:

Acute anterior uveitis occurs in 25-30% of the patients with ankylosing spondylitis and that can be the first presenting symptom of the disease.It is characterised by recurrent, unilateral sudden ocular pain with redness and photophobia. The occurrence of acute anterior uveitis is increased in the HLA-B27 positive population.

These attacks causes inflammatory debris accumulating in the anterior chamber which may cause papillary and lens dysfunction which leads to blurring of vision. In few cases glaucoma and even blindness may occur if adequate treatment is delayed but most of the time the uveitis resolves spontaneously within 3 months.

Uveitis can be treated by local corticosteroids or TNF-blocking agents like infliximab which seems to be successful in refractory uveitis [11] .

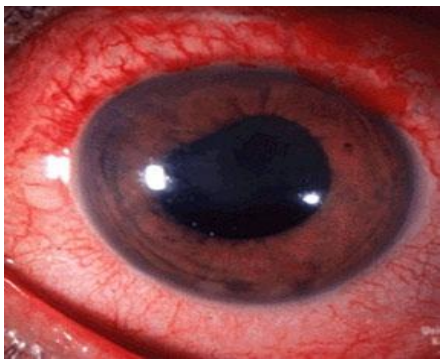


Figure 5: Anterior Uveitis in AS

Gastro – Intestinal:

Inflammatory bowel disease is described in a high percentage of patients with spondyloarthropathy (60%) and can be detected by endoscopy of the colon and terminal ileum[12]. These lesions can be divided into acute lesions resembling acute bacterial infections and chronic lesions with features of inflammatory bowel disease.

The chronic lesions are more often seen in association with AS and although these enteric mucosal lesions most of the time are clinically silent, patients with chronic lesions experience significantly more episodes of diarrhea. During follow up studies it appeared that up to 25% of these AS patients with peripheral arthritis and chronic gut inflammation eventually develop Crohn's disease[13] .

Pulmonary:

Pulmonary complications can be caused by rigidity of the chest wall and apical pulmonary fibrosis. In a retrospective study, an incidence of apical pulmonary fibrosis in AS was reported in 7%, based on plain radiography[14].This complication occurs, on average, two decades after the onset of AS, but recent studies with high resolution computed tomography (HRCT) detected interstitial lung disease in 50 –70 % of the patients with early AS, defined as a duration of < 10 years[15] patients. Cavities in the fibrotic parts can be infected by bacteria and fungi like Aspergillus.

These cavitations mimic tuberculosis in one thirds of the patients. Chronic aspergillus colonization is reported in 50-65% of patients with AS, whereas 10-30% develop an aspergillosis infection. Treatment is based on the administration of antifungal drugs with surgical resection of the cavity and removal of the fungal ball. The inflammation of costovertebral and costotransverse joints do not reduce the pulmonary function. The total lung and vital capacities are seldom reduced in AS patients, despite the diminished chest expansion, because the diaphragmatic function is not impaired .

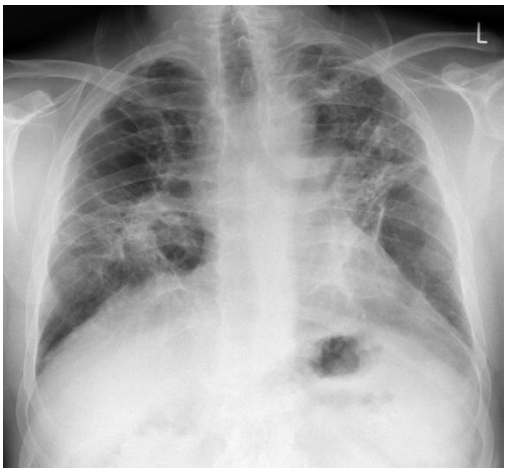


Figure 6: Chest X Ray with bilateral upper and mid zone fibrosis

RENAL:

Renal abnormalities in Ankylosing Spondylitis varies with an incidence [16] between 10-18%. These include

a.Secondary renal amyloidosis , most common in AS (62%).

b.IgA-nephropathy (30%).

c. mesangioproliferative glomerulonephritis (5%)

Other rare associations could be membranous nephropathy and Focal segmental glomerulosclerosis.

Renal amyloidosis is to be considered in case of proteinuria and renal failure in AS. In 7% amyloid can be found in abdominal fat or rectal biopsies, but most do not develop clinically significant disease. Proteinuria or impaired renal function can indicate IgA-nephropathy, which is interesting because of the increased serum IgA levels in AS patients. Cases of IgA multiple myeloma have also been reported.

Neurological:

Vertebral fractures, especially of the cervical spine, and cervical spine dislocations can cause neurological deficits after minor trauma. A slowly progressive cauda equina syndrome might occur late in the disease course as a rare complication, first described by Browie and Hauge in 1961.[17]

The symptoms are a sensory loss in the lumbar and sacral dermatomes with weakness in the legs and bowel and bladder incontinence[18]. MRI can demonstrate arachnoiditis, with characteristic enlarged dural sacs and arachnoid diverticula . One study with CT-scan also showed dural calcification. Treatment with NSAIDs or corticosteroids alone is inappropriate to improve the neurological deficit and often surgical treatment of the dural ectasia, by lumboperitoneal shunting or laminectomy is necessary.

Hormonal:

The elevated susceptibility for AS in men compared with women did suggest an etiological role for sex steroids in AS. In male patients, elevated serum testosterone and in premenopausal females lower 17β–estradiol levels were reported. It was even suggested that anti-androgenic treatment would be beneficial for AS patients[19].

However, more recent studies revealed that serum testosterone levels are not elevated in male AS patients, but previous found elevations might be explained due to the use of phenylbutazone . Therefore, no basis is provided for anti-androgenic treatment. Also, the 17β-estradiol levels in later studies did not differ between AS patients and controls. The influence of hormones like prolactin and growth hormone, which might have a pro-inflammatory effect, were recently studied in men with AS and Rheumatoid Arthritis(RA).

Cardiac Manifestations:

Cardiac involvement in Ankylosing spondylitis can occur in the form of

a. aortic valve incompetence, aortitis of the ascending aorta

b. conduction abnormalities.

c.Mitral Regurgitation

d. Myocardial involvement with Left ventricular dysfunction

e. Cardiomyopathy and Pericarditis can also occur.

Conduction Disturbances:

Inflammation and fibrosis of the membranous portion of the interventricular septum and that affecting the atrioventricular node leads to conduction disturbances[20]. The occurrence of conduction disturbances in patients with AS varies from 1-33%. It can result in any form of heart block. First degree heart block is very common among them. Sometimes patients may require pacemaker implantation in case of a complete heart block. Conduction disturbances increases with increased duration of the disease.

Aortic Regurgitation:

1 – 10% of patients with ankylosing spondylitis will have Aortic insufficiency. Age and duration of the disease increases the incidence of aortic insufficiency[21,22] . Inflammatory process affecting the aortic wall leading to fibrotic thickening and shortened aortic valve cusps and a dilatated aortic root resulting in aortic regurgitation[23,24] .

The aortic insufficiency results in volume overload to the left ventricle with eccentric hypertrophy and dilatation of the chamber. This results in increased end diastolic pressure in the left ventricle and ultimately resulting in heart failure in several years. The patient presents with chest pain and dyspnoea which often leads to Aortic valve replacement as the effective therapy[25].

The occurrence of mitral regurgitation, myocardial involvement with left ventricular dysfunction, cardiomyopathy and pericarditis in ankylosing spondylitis is rare.

Physical examination:

Blood pressure should be measured to exclude hypertension in case of renal involvement or aortic insufficiency in ankylosing spondylitis and pulse rate to detect bradycardia and irregular rhythm in case of atrioventricular conduction disturbances.

Psoriatic lesions should be looked for in the skin, nails. The skin over the ears, scalp, natal region, extension surfaces of the elbows and knees and pitting lesions of the nails since psoriatic arthritis may mimic ankylosing spondylitis.

The eyes should be examined for redness in case of pain and blurring of vision which may be caused by conjunctivitis or an attack of acute anterior uveitis. An irregular pupil may result from an attack of uveitis in the past with synechiae to the cornea or lens, which might cause glaucoma in the long term . Examination of the heart to detect a murmur caused by aortic insufficiency and in such patients collapsing pulse and peripheral signs of aortic regurgitation should be looked for and bilateral basal crepts and jugular venous pulsations and pressure should be measured in case of heart failure. Bradycardia should be looked in case of cardiac conduction abnormalities.

The chest might show signs of a limited chest expansion and crepts in case of apical fibrosis, although these lung deformities often can only be detected by radiographic procedures. The abdomen should also be examined,

but signs of inflammatory bowel disease most often are detected only with ileocolonoscopy.

Physical examination of the spine involves the cervical, thoracic and lumbar region. Cervical involvement occurs late in the disease which can result in a limited flexion, extension, rotation or lateral flexion movements. The stooping of the neck can be measured by the occiput-to-wall distance. The patient stands with the back and heels against the wall and the distance between the back of the head and the wall is measured. Eventually the neck become fixed in a flexed position.

The thoracic spine can be tested by measuring the chest expansion, the difference between deep inspiration and expiration which normally exceeds 5 cm, that is measured at the level of fourth intercostal space in men just below the breasts in women. It is age- and sex-dependent, with lower expansion in females compared with males and decreases with age.

A chest expansion of less than 5 cm is suspicious and < 2.5 cm is abnormal and raises the possibility of AS unless there is other reason like emphysema. In progressed AS, the anterior chest wall becomes flattened, shoulders become stooped, the abdomen becomes protuberant and the breathing diaphragmatic. The normal thoracic kyphosis of the dorsal spine becomes accentuated.

The costovertebral, costotransverse and manubriosternal joints should be palpated to detect inflammation which causes pain on palpation.

The lumbar spine can be tested by modified Schobers test which tests the ability of the patient to bend forward to touch the floor by the fingertips with the knees fully extended. This detects limitation of the forward flexion of the lumbar spine.

This is performed by making a mark between the posterior superior iliac spines at the 5th lumbar spinous process. A second mark is placed 10 cm above the first one and the patient is asked to bend forward with extended knees. The distance between the two marks increases from 10 to at least 15 cm in normal people, but only to 13 or less in case of AS.

Lumbar lateral flexion can be tested by the patient standing erect with the arms along side the body and by moving laterally with the fingers over the lateral side of the leg. The distance between the measurement can be repeated on the other side.

Signs of synovitis include pain, swelling, tenderness and limited motion of the joint and it should be looked for in all peripheral joints. The hips and shoulder are most often involved in one-third of the patients, and any limitations in function should be recorded early in the disease in order to detect progression later. Other joints often involved are the knees, wrists, elbows. The presentation is usually asymmetric and often monoarticular or oligoarticular.

INVESTIGATIONS:

Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP), an acute phase reactant seem to be elevated in 50-70% of the patients with an active disease. [26] These parameters show a higher correlation with peripheral involvement of ankylosing spondylitis than with spinal disease activity.

In contrast with rheumatoid arthritis, these acute phase reactants do not have a high correlation with the disease activity of AS and elevation is more often observed in case of extraspinal manifestations than in case of more axial involvement. Therefore, their value as an outcome parameter for disease activity in therapeutic trials in AS is limited.

The platelet count may also be slightly elevated and a mild normochromic normocytic anaemia, due to a chronic disease is common in 15% of the patients. Positive tests for the rheumatoid factor and ANA do not occur more often than in healthy controls. The HLA-B27 antigen is present in the majority of the AS patients, but this test is inappropriate to confirm the diagnosis, which is primarily based on history, physical examination and radiographic evidence of sacoiliitis. In adolescent patients where the radiographic confirmation of sacroiliitis can be difficult, HLA-B27 testing could be helpful to establish the diagnosis.

Raised alkaline phosphatase, primarily derived from bone and serum IgA levels are common in AS. The urine might show protein or erythrocytes in case of renal involvement.

Radiology

The radiograph of the pelvis is necessary to assess the sacroiliac joints (SI), which might show signs of sacroiliitis, an obligatory sign for the diagnosis of AS. The severity of this sacroiliitis can be graded from 0 (no abnormalities) to grade 4 (complete ankylosis of the SI-joints). At early stages of the disease, signs of sacroliitis can be detected with CT and MRI before the abnormalities are present at the plain radiograph of the pelvis.

Also, the vertebral column often shows characteristic changes, like bony sclerosis with squaring of the vertebral bodies and ossification of the annulus fibrosis with syndesmophytes. This might lead to fusion of the vertebral column with a classical Bamboo-spine aspect on the radiograph of the lumbar region. Involvement of the hip and shoulder joints with joint space narrowing can be detected by conventional X Rays.

Figure 7: Bamboo spine appearance of vertebral column in AS

Grading of Sacroiliitis by plain radiographs according to the modified New York Criteria:

Grade 0: Normal

Grade 1: Suspected changes

Grade 2: Small areas with erosions or sclerosis without joint width alteration, minimal abnormality

Grade 3: Advanced sacroiliitis with erosions, widening, sclerosis or partial ankylosis

Grade 4: Total ankylosis

Magnetic Resonance Imaging: It can detect early cartilage abnormalities and bone marrow oedema.

Other investigations to find the systemic manifestations include:

Cardiac:

Chest X Ray – May show cardiomegaly. Aortic regurgitation and mitral regurgitation occurring in ankylosing spondylitis can be associated with Left ventricular hypertrophy and enlargement of other cardiac chambers.

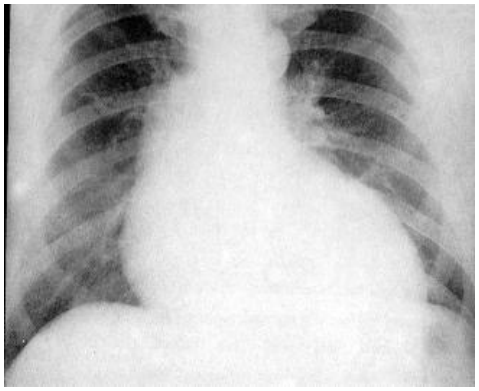


Figure 8: Chest X Ray Showing cardiomegaly in aortic regurgitation

ECG – Cardiac conduction disturbances especially atrioventricular blocks can be detected. Most common is the first degree AV block.

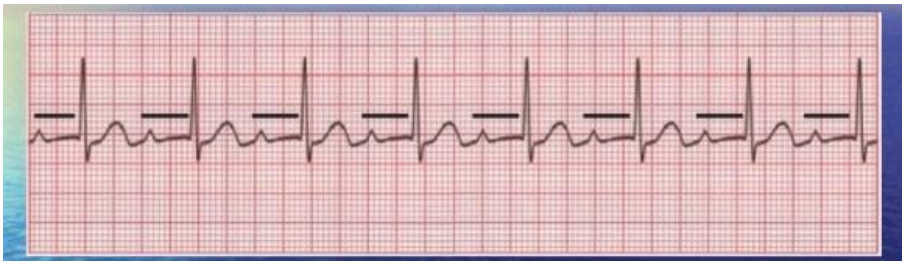


Figure 9: ECG with First degree AV Block

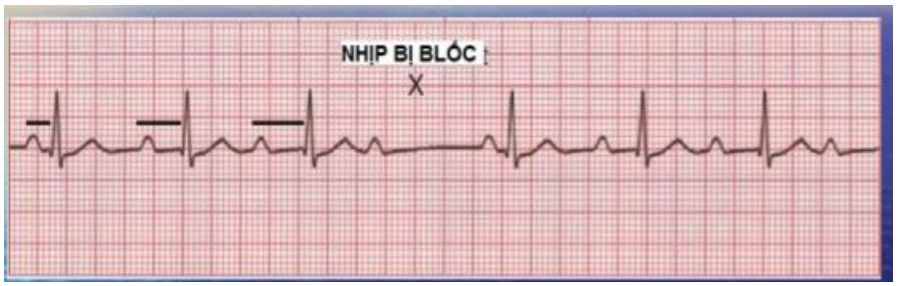


Figure 10: ECG with Second degree AV Block (Type 1)

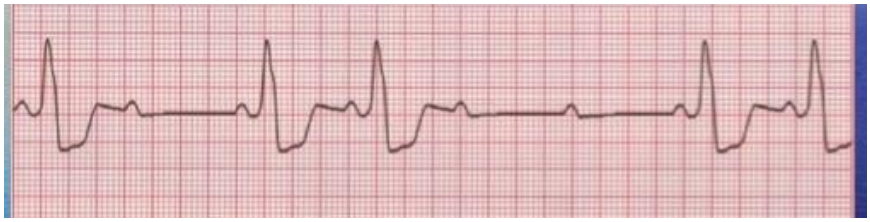


Figure 11: ECG with Second degree AV Block (type 2)

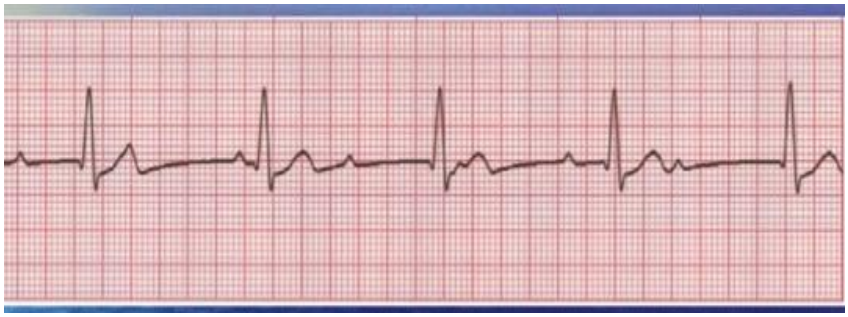


Figure 12: ECG with Third degree AV Block

Echocardiogram – Can detect reguritant lesions, left ventricular hypertrophy, aortic root dilatation, left ventricular diastolic dysfunction, regional wall motion abnormalities in case of ankylosing spondylitis. Most common is the aortic regurgitation which can be mild, moderate, severe according to central jet velocity, Regurgitant orifice area, regurgitant fraction described later.

Figure 13: Echocardiogram in Aortic Regurgitation

Figure 14: Aortic root dilatation

Pulmonary:

Chest X Ray - Apical fibrosis can be detected

HRCT Chest – Reveals if any interstitial lung disease

Pulmonary Function test – Shows restrictive pattern of lung disease

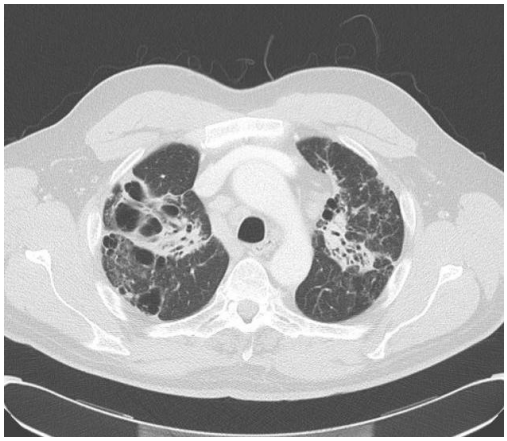


Figure 15: CT Chest with Bilateral upper lobe fibrosis

Ophthalmic examination, Renal parameters, relevant neurological investigations should be done in cases of eye, renal, neurological manifestations respectively. Duodenoscopy and colonoscopy in cases of suspected inflammatory bowel disease.

Diagnostic criteria:

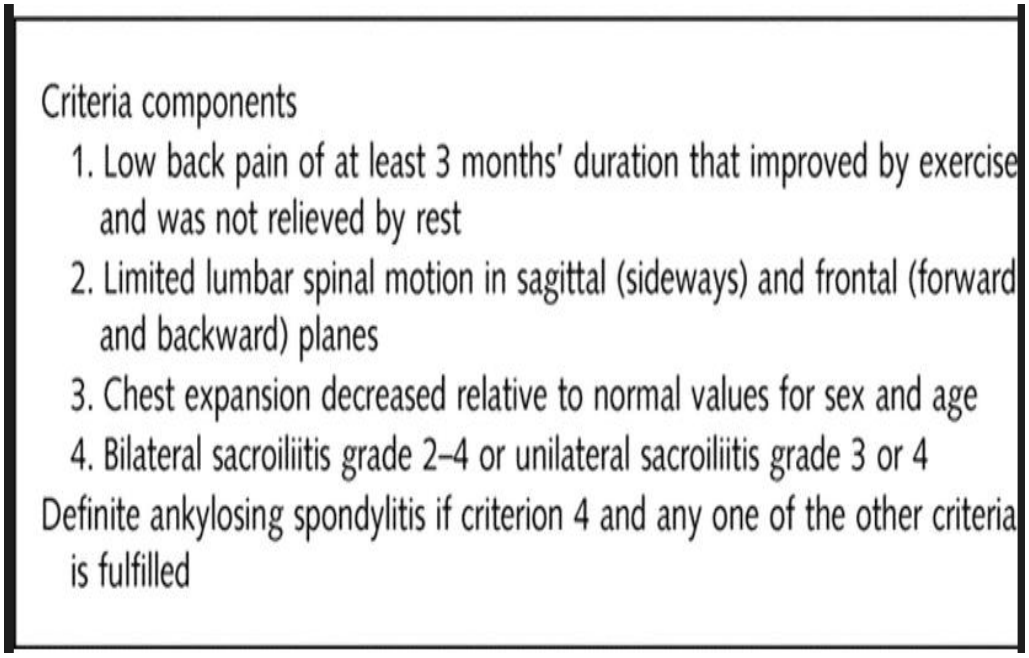
The Assessment of SpondyloArthritis International Society (ASAS) criteria:

Table 1: ASAS CRITERIA

Patient with a ≥3-month history of back pain, and aged ≤45 years at onset		
Sacroiliitis on imaging* Plus At least one other SpA feature**	Or	HLA-B27 positivity Plus At least two other SpA features**
*Sacroiliitis on imaging: Active (acute) inflammation on MRI, highly suggestive of sacroiliitis associated with SpA Or Definite radiographic sacroiliitis according to modified New York criteria		** SpA features: Inflammatory back pain Arthritis Enthesitis (heel) Uveitis Dactylitis Psoriasis Crohn's disease/colitis Good response to non-steroidal anti-inflammatory drugs Family history of SpA HLA-B27 positivity Elevated C-reactive protein levels
ASAS: Assessment of SpA International Society; HLA-B27: human leukocyte antigen-B27; SpA: spondyloarthritis.		

The characteristics of inflammatory back pain in AS are insidious onset of pain with onset in <40 years of age, which is improved with exercise and not so with rest, morning stiffness>30 minutes and pain more during night with alternating buttock pain.

Table 2: MODIFIED NEW YORK CRITERIA(1984)



Criteria components

1. Low back pain of at least 3 months' duration that improved by exercise and was not relieved by rest
2. Limited lumbar spinal motion in sagittal (sideways) and frontal (forward and backward) planes
3. Chest expansion decreased relative to normal values for sex and age
4. Bilateral sacroiliitis grade 2–4 or unilateral sacroiliitis grade 3 or 4

Definite ankylosing spondylitis if criterion 4 and any one of the other criteria is fulfilled

Grades of sacroiliitis have been described earlier.

The other criterias which were in use for ankylosing spondylitis were European Spondyloarthritis Study Group (ESSG) Criteria, ROME Criteria and Amor Criteria.

Differential Diagnosis

The diagnosis of AS can be confirmed by the ASAS criteria as described earlier. AS belongs to the group of diseases called Spondyloarthropathies (SpA), which have the inflammatory back pain as a common feature.

Other types of Spondyloarthropathies include psoriatic arthritis, reactive arthritis, inflammatory bowel disease (IBD), juvenile spondylarthropathy and group of undifferentiated spondyloarthropathies. The majority of affected individuals with SpA possess the HLA-B27 antigen.

Psoriatic arthritis occurs in 5-7% of the people with psoriasis. The psoriatic arthritis presents as a monoarthritis or oligoarthritis resembling the reactive arthritis pattern, or as an symmetrical polyarthritis like rheumatoid arthritis (RA), but with involvement of the DIP-joints in stead of the PIP-joints in RA and without a positive rheumatoid factor. Axial disease occurs in about 5% of the psoriasis patients. Axial involvement may occur independent from peripheral arthritis and is often asymptomatic, but symptoms of inflammatory back pain or chest wall pain may be present. Sacroiliitis is observed in one-third of the patients and frequently asymmetric. Spondylitis may occur without sacroiliitis and may result in fusion of the spine. Enthesitis is common, especially in the oligoarticular form of the disease. The radiographic features of the spine in case of psoriatic spondylitis show more or less random

syndesmophyte formation, whereas in AS, syndesmophytes form in a more ascending fashion[27].

Peripheral arthritis occurs in 10-20% of patients with IBD like ulcerative colitis and Crohns disease.Knees, ankles and feet are most frequently involved. Large-joint effusions, especially of the knee are common. In 10% of the patients with IBD sacroiliitis or spondylitis occur and is often asymptomatic. The course of the spondylitis is independent of the active bowel inflammation.

Reactive arthritis refers to a mono-or oligoarthritis, which occurs after an infection of the genitourinary (with Chlamydia trachomatis), gastrointestinal tract (with Salmonella, Shigella, Yersinia or Campylobacter bacteria) or sometimes after a respiratory infection with Chlamydia pneumoniae. The arthritis usually occurs two to four weeks after the primary infection, as an urethritis or a period of diarrhoea. Conjunctivitis, with crusting of the eyelids in the morning, can accompany the urethritis, but an acute anterior uveitis might also occur. The combination of arthritis, conjunctivitis and urethritis is also known as the Reiters syndrome. The joint involvement is asymmetrical and located predominantly in the knees, ankles, and small joints of the feet, but joints of the upper extremities (wrist, elbows and hand joints) can also be affected. The large joints show signs of synovitis whereas the small joints of the hands and feet present as sausage digits or dactylitis. The course of reactive arthritis is self limiting with 3 to 12 months in the majority of the patients and the treatment consists of Non-steroidal anti-inflammatory drugs (NSAIDs) whereas antibiotic treatment is not indicated.

Rheumatoid arthritis (RA) can manifest with an mono-or oligo-articular onset, but has most often a symmetrical polyarthritis. RA can be distinguished from AS by the absence of inflammatory back pain and the presence of the positive rheumatoid factor, in 60-70% of the patients and because it is more often associated with an increased ESR or CRP. The radiological features of RA, with erosions of the small joints of hands and feet, differ from AS.

Juvenile spondylarthropathy applies to a diagnosis made before the age of 16 and belongs to the group of Juvenile Idiopathic Arthritis (JIA). Most patients are boys and HLA-B27 positive and the tests for the rheumatoid factor and anti-nuclear antibodies (ANA) are usually negative. The symptoms mainly involve arthritis of the large joints of the lower extremities, especially the hip joint, which predicts a severe course of the disease. Enthesitis is common, as well as lower back or buttock pain. Acute anterior uveitis occurs in 5-10% of the patients. Plain radiographs of the sacroiliac joints and the lumbar spine often do not show abnormalities for many years. Treatment is based on NSAIDs and sulfasalazine is added in case of persistent arthritis. Diagnosis resembling the complaints of AS are other syndromes or diseases that effect the spine, like a prolapsed intervertebral disc, fibromyalgia, spinal tumours, like chordoma or ependymoma, bone tumours, like osteoid osteoma, plasmacytoma, bone metastases or leukemic infiltration and infections of the spinal or sacroiliac joints like tuberculosis and brucellosis. Metabolic bone diseases like osteomalacia, hypophosphatemia and rickets can also cause back pain. The noninflammatory back pain is, in most cases, aggravated by activity and

relieved by rest and is not associated with a limited chest expansion or a limited lateral flexion of the lumbar spine.

Diffuse idiopathic skeletal hyperostosis (DISH or Forestier's disease) can resemble AS because of the stiffness of the spine due to hyperostosis of the anterior longitudinal ligaments and bony attachments of the tendons. Occasionally the SI-joints show hyperostotic changes resembling sacroiliitis, but in most cases of DISH this feature is absent. However, in contrast with AS, the onset of the disease is at a later age (over 50), there is no association with HLA-B27 and there are more flowing ligamentous ossifications but less syndesmophyte formations.

Outcome of the disease:

The disease outcome is favourable in many patients whereas in approximately one third of the patients end with disabling deformities. A few studies have showed that the outcome of ankylosing spondylitis can be predicted by several disease characteristics during the first ten years of the disease.[28,29]. Predictors of a severe outcome are arthritis of the hip joint, an increased erythrocyte sedimentation rate, (ESR > 30mm/hr), peripheral arthritis and a juvenile onset (<16 years).

The rate of radiological progression appears to be constant during the several decades of the disease duration and is not higher in the first decade as once previously thought. However, most patients who have mild spinal restriction after the first decade of their disease do not progress to severe spinal

involvement during later years. Because AS starts at a young age, the socioeconomic consequences are high. Apart from the physical complaints, many patients struggle with work disability. This subject was recently studied by Boonen in the Netherlands. The age and sex adjusted risk of work withdrawal was 3 times higher in AS compared with the figures of the general Dutch population.

The stage of the disease at the time of diagnosis and the delay of appropriate treatment also influence the outcome of the disease. Women appear to have a later age of onset and a milder disease compared with men. The majority of AS patients possess the HLA-B27 antigen (> 95%), which is found to be associated with the onset of the disease. The relationship of this antigen with disease severity is less known.

In HLA-B27-negative patients a later age of onset, and less frequent occurrence of acute anterior uveitis and less familial aggregation was described[30]. Also, HLA-B27 homozygous individuals seem to develop a more severe disease compared with HLA-B27 heterozygotes. There are conflicting data regarding mortality in patients with AS. One population-based study, showed no difference in mortality between males with AS and the general male population[31].

Other studies indicated that mortality in AS patients seen at referral centers was higher than expected with standardized mortality ratio's (SMR) of approximately 1.7 (range 1.5-1.9). This might be due to a linear relation

observed between disease severity[32] and mortality as well as associations found between disease duration and mortality[33]. Among older patients X-ray treatment, which was used until 1960, might be a factor in the increased mortality risk of 4.8 due to leukemia and other types of cancer among these patients.

Treatment:

Treatment for ankylosing spondylitis includes certain exercises, physiotherapy and medications. Although these measures offer no cure, the morbidities of the disease can be reduced. It mainly reduces the pain, stiffness, inflammation and deformities.

Flexibility and strengthening exercises can control pain and maintain mobility and reduces the stiffness if done regularly. Deep breathing exercises can enhance the lung capacity. A physical therapist can help to use heat and cold to help control your pain and stiffness. Heat can help with relaxation and pain relief and cold can help reduce inflammation.

Patients major complaint of pain can be relieved by medications like non – steroidal anti inflammatory drugs like Ibuprofen, Naproxen, Diclofenac. These drugs can reduce pain by decreasing the inflammation. Dosage should be monitored and lowest possible dose should be prescribed. Other pain relievers are Paracetamol, Codeine in severe cases.

If the symptoms are not controlled with these medications then Anti – Tumour Necrosis Factor (TNF) medications can be initiated. They work by

preventing TNF, which is a chemical produced by inflammed tissues and suppresses joint inflammation. These medications are given as injections and they are Adalimumab, Etanercept, Golimumab, Infliximab. These medications can interfere with the immune mechanisms and can cause serious infections.

Nice Guidelines:

The National Institute for Health and Care Excellence (NICE) has produced guidance about the use of anti-TNF medication for AS.

NICE states that anti TNF medications may only be used if:

- Ankylosing spondylitis diagnosis is confirmed.
- The level of pain after assessing twice 12 weeks apart has not improved.
- The condition has not improved after testing with BASDAI twice,12 weeks apart.
- Four weeks of highest possible dose of 2 or more NSAIDs have not reduced the symptoms.

After 12 weeks of treatment with anti-TNF medication, the pain score and BASDAI will be tested again to see if the patients have enough improvement to make continuing therapy worthwhile. If they have improvement of symptoms, treatment can be continued and tested every 12 weeks.

If there is no enough improvement after 12 weeks, the test can be repeated at a later date and these medications can be stopped if there is no relief of symptoms.

Corticosteroids:

These drugs have a powerful anti – inflammatory action. These drugs can be injected directly into the inflamed joint and the joint should be made to rest for upto 48 hours. It can be used as injection or tablet forms.

It is wise to have a corticosteroid injection up to three times in one year, with at least three months between injections in the same joint because of side effects such as:

- infection with response to the drugs
- Depigmentation of the skin
- Rupture of the tendon near the joint

Other drugs like Disease Modifying Anti-Rheumatic Drugs(DMARDS) like Sulfasalazine and Methotrexate can be used to reduce pain and inflammation.

Surgery:

Surgery is not indicated in many people with ankylosing spondylitis.

However, in cases where a joint has become severely damaged, joint replacement surgery may be recommended to improve pain and movement in the affected joint like hip, knee joint replacement. In some patients corrective surgeries of the spine may be required.

MATERIALS & METHODS

METHODOLOGY:

The study is undertaken on the patients approaching the outpatient department as well as the Inpatients of the Coimbatore Medical College Hospital, Coimbatore during the period of study (i.e. July 2015 to July 2016). A total of fifty (50) subjects who had approached the Rheumatology Department in the Hospital, and having satisfied the ASAS criteria were selected for the study. These patients were compared with another fifty (50) age and sex matched control group, who had come to the OP department for non-specific complaints. The control group was selected on a random basis.

SELECTION CRITERIA

(a) Inclusion Criteria

- Adult patients (both sex) between the age group of 18 to 60
- Patients satisfying Assessment of Ankylosing Spondylitis International Society (ASAS) criteria for Ankylosing Spondylitis

(b) Exclusion Criteria

- Pregnant women
- Minors (below the age of consent)
- Persons suffering from congenital heart diseases
- Persons suffering from Psoriatic Arthritis
- Persons suffering from Rheumatic valvular heart diseases
- Persons not capable of giving consent (psychiatric patients)

- Persons unwilling to undergo the study (who refused to consent)

TYPE OF STUDY

Cross sectional study

All patients are evaluated with:

Detailed history

Age, sex, duration of the disease, extra axial joint involvement, extraarticular manifestations, presence of other systemic diseases, response to anti inflammatory drugs, family history of ankylosing spondylitis were all documented.

Examination

Examination of all joints was done and cardiac examination was done to find for cardiomegaly, cardiac murmurs. Ophthalmic and other systemic examination was done.

Investigations

Routine investigations like Blood haemoglobin, Renal function test and blood sugar estimation were done.

C Reactive Protein was estimated using latex agglutination kit.

Erythrocyte sedimentation rate was measured.

Radiography:

X Ray B/L sacroiliac joint:

X Ray of peripheral joints were done.

Chest X Ray PA view was done to look for cardiomegaly

Electrocardiogram:

A 12 lead electrocardiogram was taken for all the cases and controls. Atrio ventricular blocks were found out by looking at the PR intervals and the proceeding QRS complexes, Bundle branch block and fascicular block were interpreted by looking at the QRS complexes in the specific leads. Chamber hypertrophies were also noted.

Echocardiogram:

With the patient in supine and left lateral position using a Hewlett Packard Sonos 2500 scanning machine, M mode, 2 dimensional and Doppler echocardiography were performed.

Cardiac position, cardiac chambers, Atrial and ventricular septae, valves, pericardium, great vessels, ejection fraction, peak velocities across the valves, trans valvular mean gradient, grading of regurgitations and aortic root diameter were noted.

Grading of Aortic Regurgitation (AR) by echocardiography is done according to the following measures:

Parameters	Mild AR	Moderate AR	Severe AR
Jet width	<25% of LVOT	25 – 64% of LVOT	≥65% of LVOT
Vena contracta	<0.3 cm	0.3 – 0.6 cm	>0.6 cm
RVol	<30 ml/beat	30 – 59 ml/beat	≥60 ml/beat
RF	<30%	30% - 49%	≥50%
ERO	<0.10 sq.cm	0.10 – 0.29 sq.cm	≥0.3 sq.cm

Grading of Mitral Regurgitation (MR) by echocardiography is done by the following measures:

Parameters	Mild MR	Moderate MR	Severe MR
Central jet	<20% LA	20% - 40%	>40%
Vena contracta	<0.3cm	0.4 – 0.7cm	>0.7cm
RVol	-	<60 ml	≥60 ml
RF	-	<50%	≥50%
ERO	-	<0.40 sq.cm	≥0.40 sq.cm

Left ventricular diastolic dysfunction is assessed by Echocardiogram with peak Early (E) and Late (A) trans mitral filling velocities and their ratio (E/A).

Statistical analysis:

The data were reported depending on their distribution as Mean +/- Standard deviation or the median. Between groups, the differences in quantitative variables were assessed by means of the unpaired t test.

Comparsion between groups was made by the Non parameteric Mann - whitney test. Differences in categoric variables were assessed by Chi-square test between groups.

A p value of <0.05 using a two-tailed test was taken as being of significance for all statistical tests. All data were analysed with a statistical software package (SPSS, version 16.0 for windows).

OBSERVATION & RESULTS

OBSERVATION AND RESULTS

The study is undertaken on the patients approaching the outpatient department of the Rheumatology department and in the inpatients of Coimbatore Medical College Hospital during the period of study (July 2015 to July 2016). A total of fifty patients who had satisfied the ASAS criteria were selected for the study. These patients were compared with another fifty control group who came to the OP Department for non – specific complaints. The control group was selected on a random basis.

Table 3: Mean age of cases and controls

Study Groups	Mean [Years]	SD	95% CI for Mean		Minimum	Maximum
			Lower	Upper		
Cases	38.1	3.1	37.2	39.0	33	44
Control	38.3	3.9	37.2	39.4	32	45
Total	38.2	3.5	37.5	38.9	32	45

In the study group the mean age group of patients with AS was 38.1 years with a standard deviation of 3.1 years and that of the control group was 38.3 years with standard deviation of 3.9 years. The youngest patient was 32 years and oldest was 45 years among the study groups.

Chart 1: Mean age of cases and controls

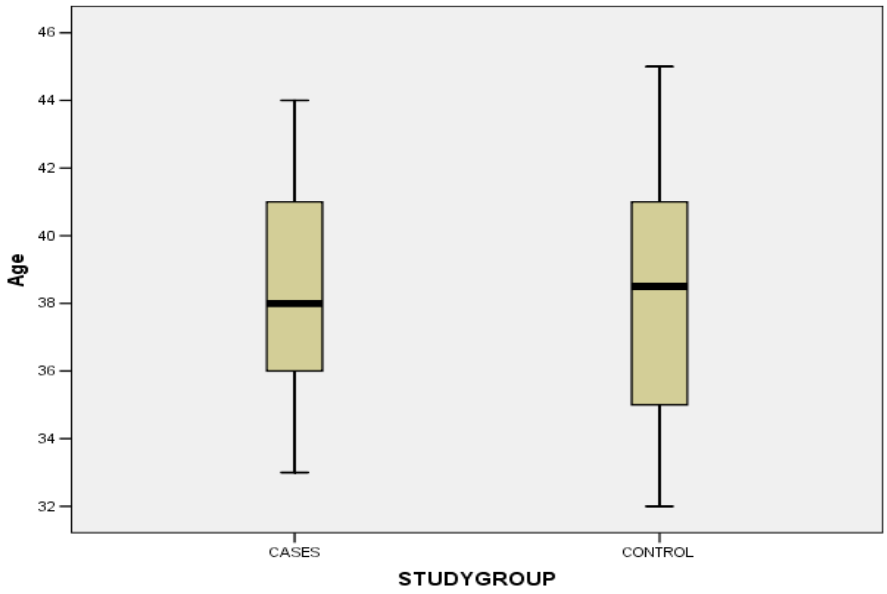
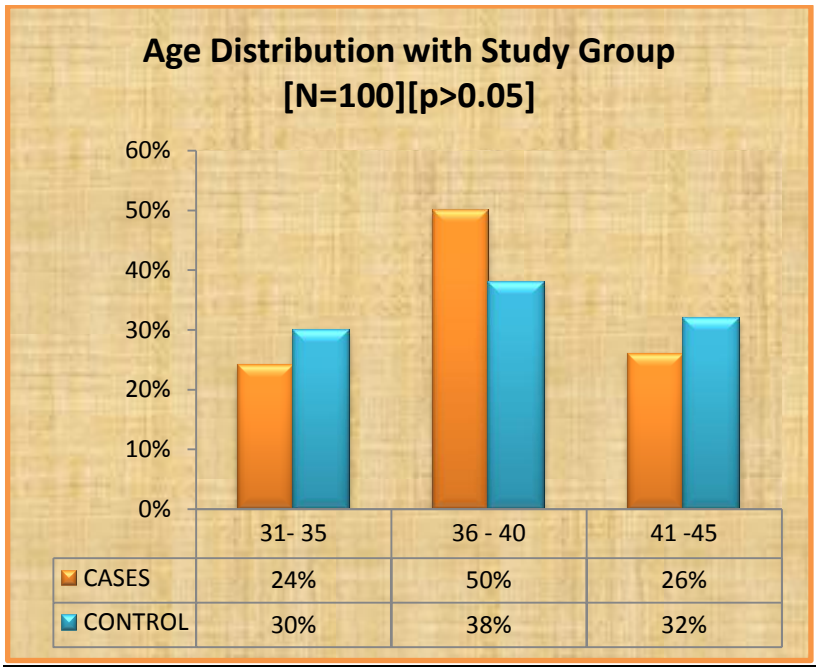


Table 4:AGE DISTRIBUTION IN STUDY GROUPS

	STUDYGROUP			
AGE	CASES	CONTROL	TOTAL	(%)
31- 35	12	15	27	27%
36 – 40	25	19	44	44%
41 -45	13	16	29	29%
TOTAL	50	50	100	

Chart 2: Age distribution in the study groups

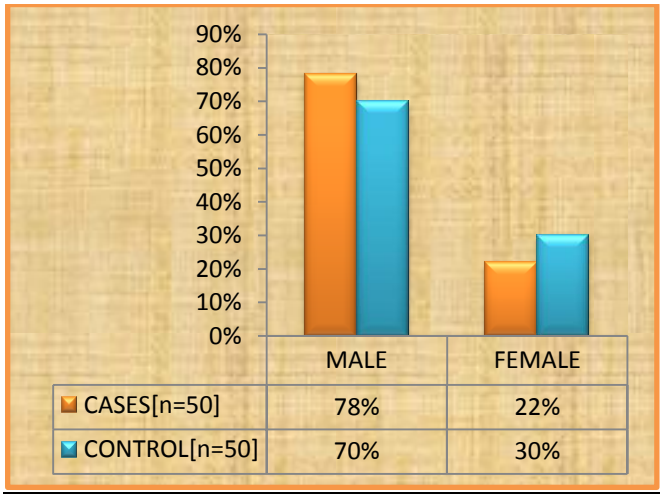


In both the cases and controls of the study groups, more number of people lie between the age group of 36 – 40 years. 50% of the cases and 38% of the controls lie in this age group. The remaining persons lie equally on either side in both the cases and the controls.

Table 5: Gender Distribution in the Study Groups

	STUDYGROUP			
GENDER	CASES	CONTROL	TOTAL	(%)
MALE	39	35	74	74%
FEMALE	11	15	26	26%
TOTAL	50	50	100	

Chart 3: Gender distribution in the cases and controls

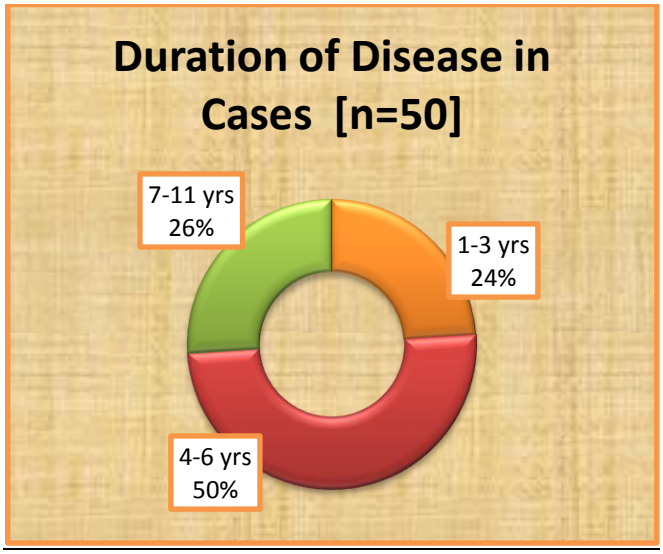


Males are more commonly affected with Ankylosing Spondylitis with 39 male cases (78%) and 11 female cases(22%). Control group also have a more number of males with 35 males and 15 females.

Table 6: Duration of disease(AS) in cases

Duration	n	(%)
1- 3 yrs	12	24%
4-6 yrs	25	50%
7-11 yrs	13	26%
Total	50	100%

Chart 4: Duration of disease (AS) in cases

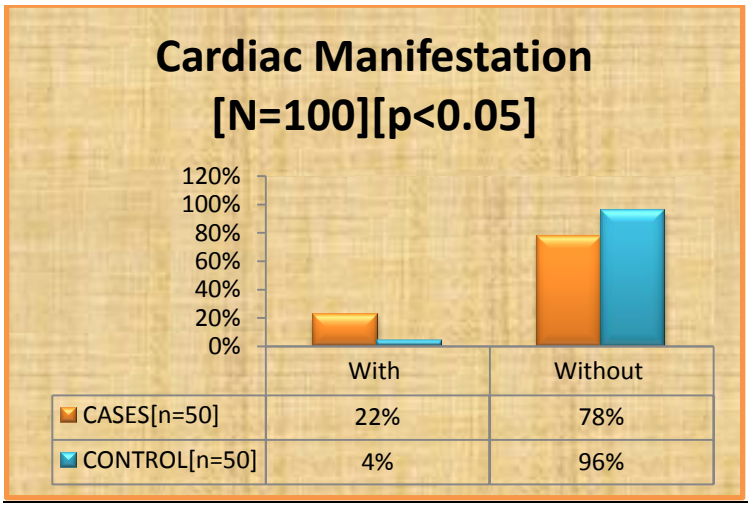


The duration of the disease varies between 1 and 11 years. Half of the cases lie within the duration of 4-6 years (50%). The remaining half is nearly equally shared by the duration of disease of 1-3 years(24%) and 7-11(26%) years.

Table 7:Cardiac manifestations in study groups

Cardiac Manifestation	STUDYGROUP		TOTAL	(%)
	CASES	CONTROL		
With	11	2	13	13%
Without	39	48	87	87%
TOTAL	50	50	100	

Chart 5: Cardiac manifestations in study groups

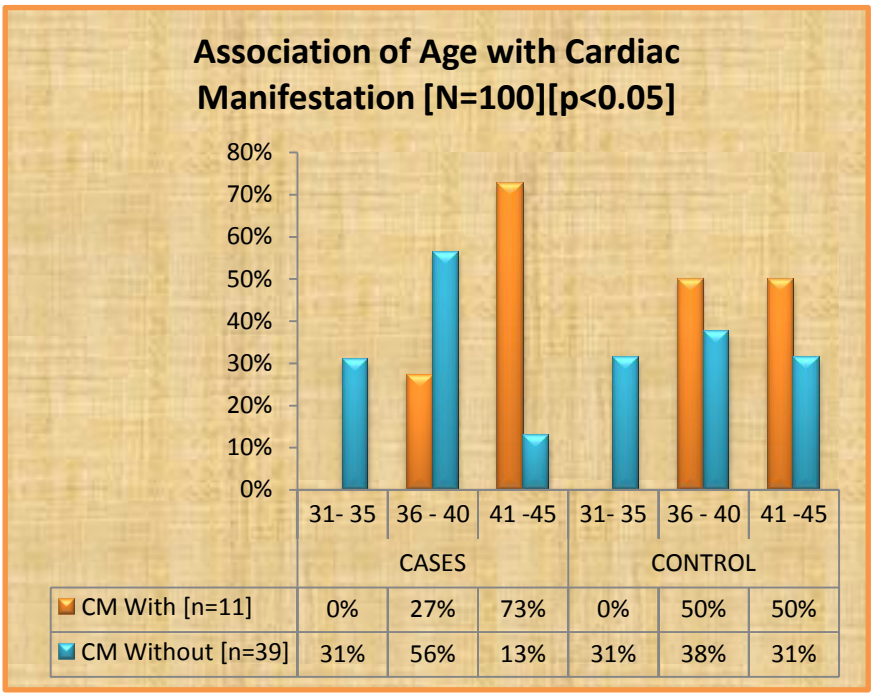


Cardiac manifestations in number of cases and controls revealed that the manifestations occurred in 11 (22%) out of 50 cases and 2 out of 50 controls (4%) in the study group.

Table 8:.Age in relation to the cardiac manifestations in the study groups

STUDYGROUP	Age	Cardiac Manifestations				Sig
		With	Without	Total	(%)	
CASES	31- 35	0	12	12	24%	<0.05
	36 - 40	3	22	25	50%	
	41 -45	8	5	13	26%	
	Total	**11**	**39**	**50**	**100%**	
CONTROLS	31 - 35	0	15	15	30%	>0.05
	36 - 40	1	18	19	38%	
	41 -45	1	15	16	32%	
	Total	**2**	**48**	**50**	**100%**	

Chart 6: Age in relation to the cardiac manifestations in the study groups

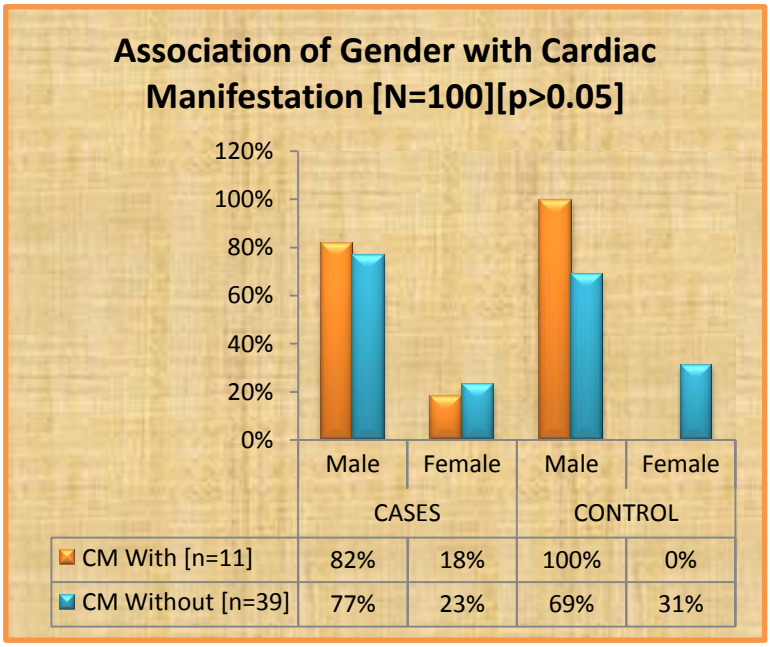


When the occurrence of cardiac manifestations in AS were divided according to the age among the cases, it was found that 73% of cardiac manifestations were found in the age group of 41 – 45 years, 27% in the age group of 36 – 40 years and none in the age group of 31 -35 years. This showed that Cardiac manifestations occurs with increasing age with a statistical significance (P>0.05) whereas it is not so in the control group.

Table 9: Gender in relation to Cardiac Manifestations in study Groups

		Cardiac Manifestations				
STUDYGROUP	**Gender**	**With**	**Without**	**Total**	**(%)**	**Sig**
CASES	Male	9	30	39	78%	>0.05
	Female	2	9	11	22%	
	Total	**11**	**39**	**50**	**100%**	
CONTROL	Male	2	33	35	70%	
	Female	0	15	15	30%	
	Total	**2**	**48**	**50**	**100%**	

Chart 7: Gender in relation to Cardiac Manifestations in study Group

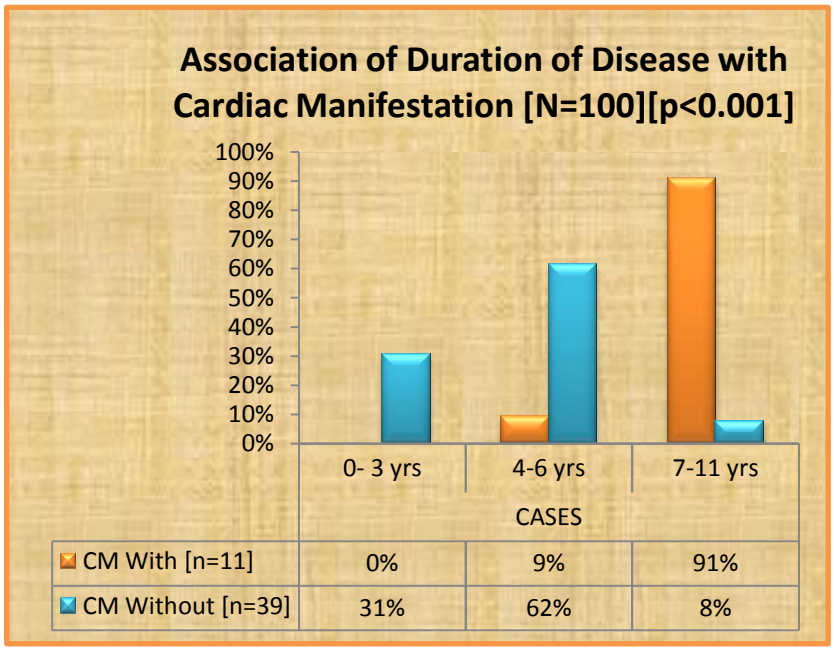


In the association of gender with cardiac manifestations it was found that males (82%) are more commonly involved than the females (18%) among the cases in the study group

Table 10. Duration of Disease(AS) in relation to Cardiac Manifestations in study Groups

STUDYGROUP	Duration	With	Without	Total	(%)	Sig
CASES	0- 3 yrs	0	12	12	24%	<0.001
	4-6 yrs	1	24	25	50%	
	7-11 yrs	10	3	13	26%	
	Total	**11**	**39**	**50**	**100%**	

Chart 8: Duration of Disease(AS) in relation to Cardiac Manifestations in study Groups

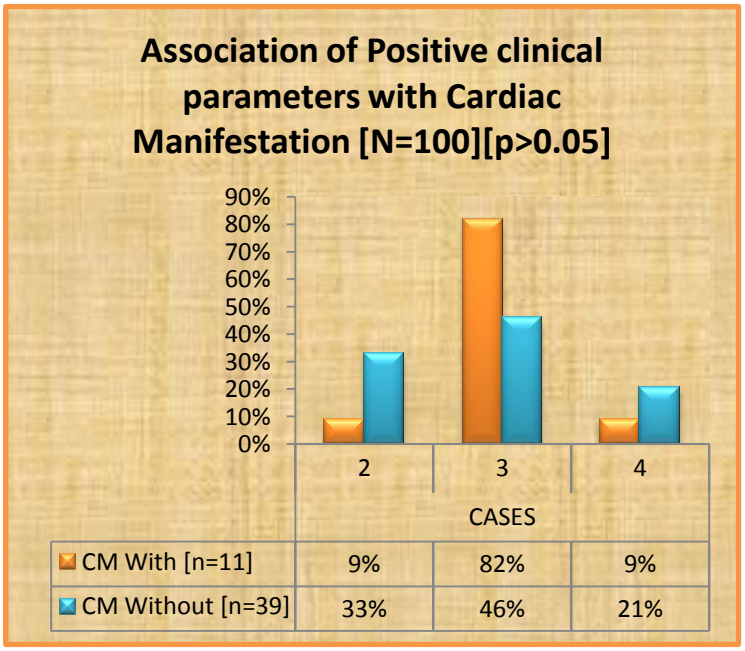


Longer duration of the disease was significantly associated with the occurrence of cardiac manifestations with 91% in those with the duration between 7-11 years, 9% in those between 4-6 years and none among those with duration of AS < 4 years which was statistically highly significant.

Table 11: Number of Positive Clinical Parameters in relation to Cardiac Manifestations in study Groups

STUDYGROUP	No of clinical	Cardiac Manifestations				
		With	Without	Total	(%)	Sig
CASES	2	1	13	14	28%	
	3	9	18	27	54%	>0.05
	4	1	8	9	18%	
	Total	**11**	**39**	**50**	**100%**	

Chart 9: Number of Positive Clinical Parameters in relation to Cardiac Manifestations in study Groups

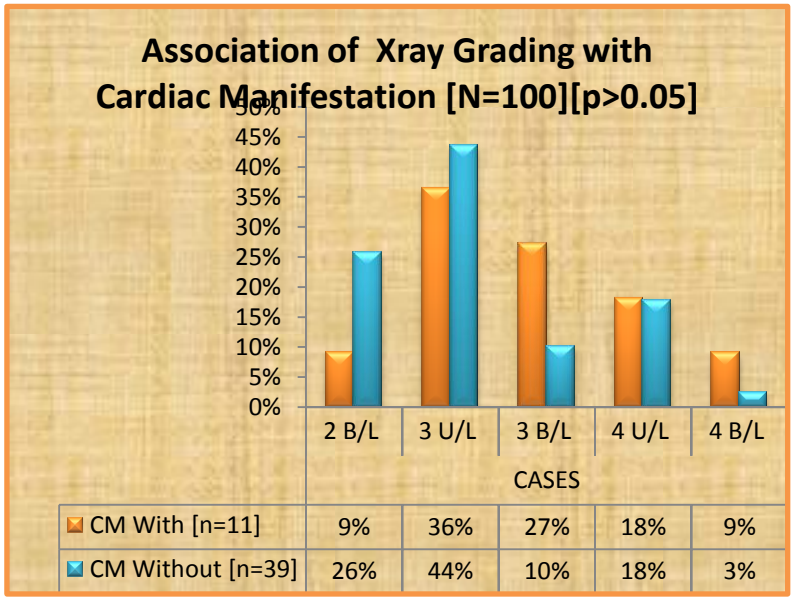


The number of clinically positive parameters of AS in cases with and without cardiac manifestations is not statistically significant.

Table 12:Grading by X ray imaging in relation to Cardiac Manifestations in study Groups

STUDYGROUP	X ray Grading	Cardiac Manifestations				
		With	Without	Total	(%)	Sig
CASES	2 B/L	1	10	11	22%	
	3 U/L	4	17	21	42%	
	3 B/L	3	4	7	14%	
	4 U/L	2	7	9	18%	>0.05
	4 B/L	1	1	2	4%	
	Total	**11**	**39**	**50**	**100%**	

Chart 10: Grading by X ray imaging in relation to Cardiac Manifestations in study Groups

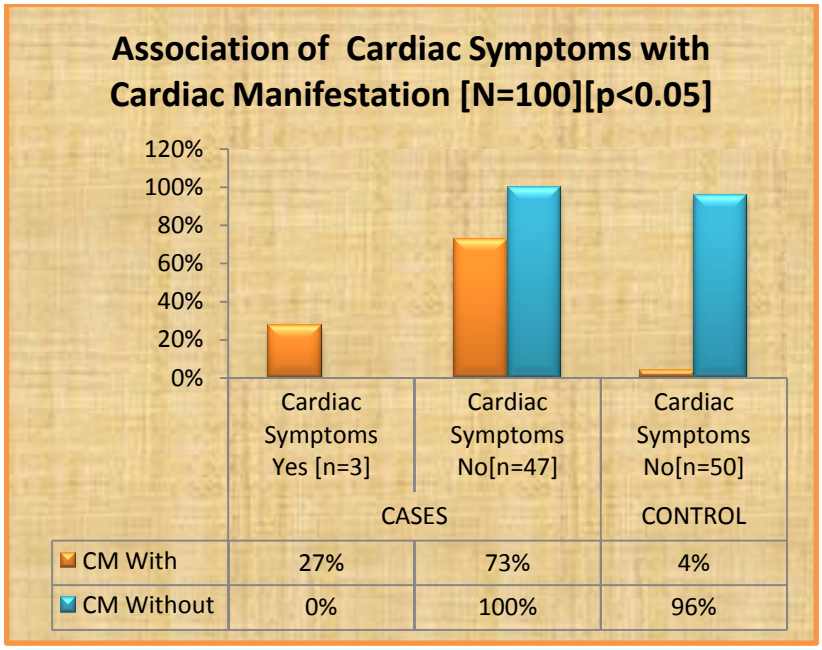


Cardiac manifestations in association with X Ray imaging by grading of sacroiliitis in AS is not found to be statistically significant. 36% of the cases with cardiac manifestations have 3 unilateral grading which is more than that of 3 bilateral, 4 unilateral and 4 bilateral.

Table 13: Cardiac Symptoms in relation to Cardiac Manifestations in study Groups

STUDYGROUP	Cardiac Symptoms	Cardiac Manifestations			
		With	Without	Total	(%)
CASES	YES	3	0	3	6%
	NO	8	39	47	94%
	Total	**11**	**39**	**50**	**100%**
CONTROLS	NO	2	48	50	100%
	Total	**2**	**48**	**50**	**100%**

Chart 11: Cardiac Symptoms in relation to Cardiac Manifestations in study Groups

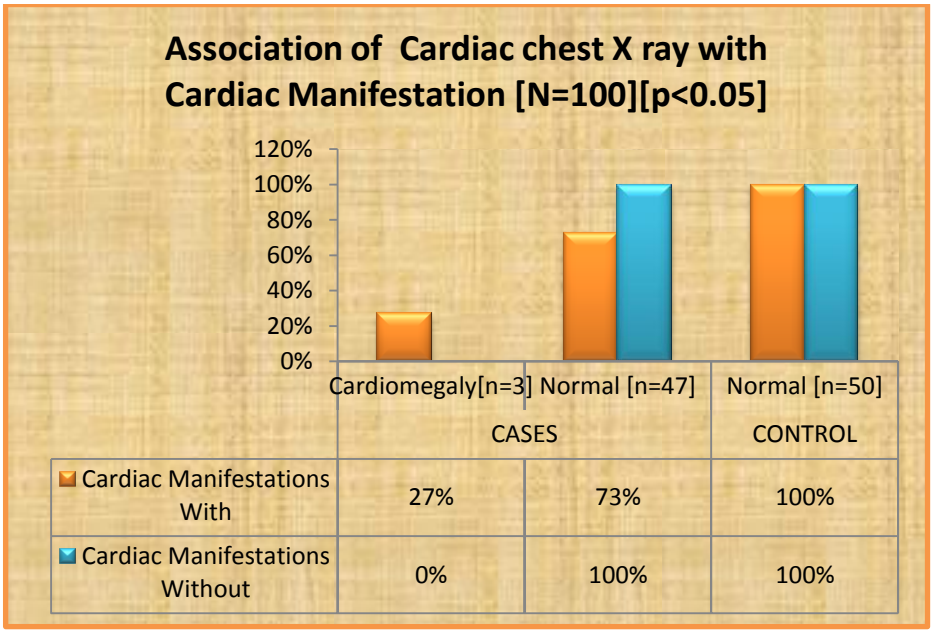


Cardiac symptoms were found in 27% of the cases with cardiac manifestations and not found in 73% of the cases with cardiac manifestations.

Table 14: Chest X ray in relation to Cardiac Manifestations in study Groups

STUDYGROUP	Chest X ray	Cardiac Manifestations With	Without	Total	(%)
CASES	Cardiomegaly	3	0	3	6%
	Normal	8	39	47	94%
	Total	**11**	**39**	**50**	**100%**
CONTROLS	Normal	2	48	50	100%
	Total	**2**	**48**	**50**	**100%**

Chart 12: Chest X ray in relation to Cardiac Manifestations in study Groups

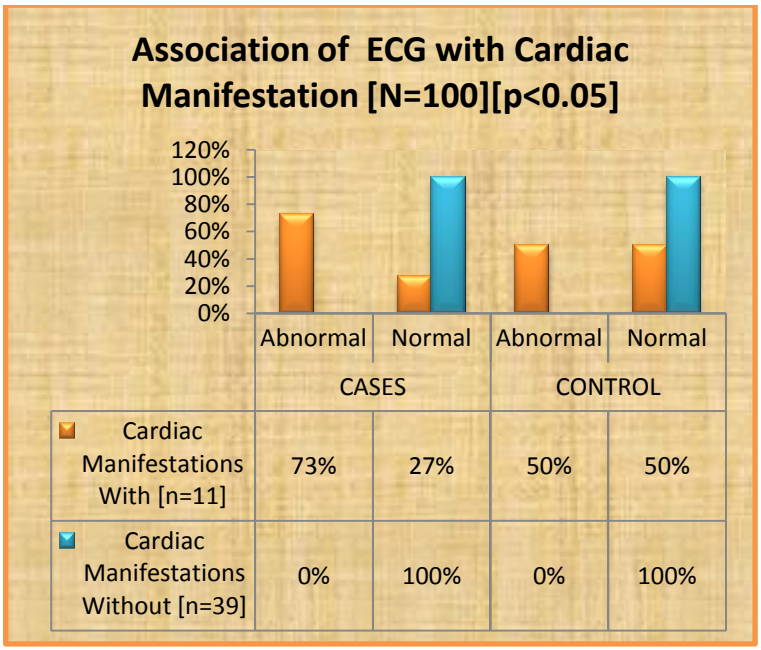


Chest X Ray showed cardiomegaly in 27% of the cases with cardiac manifestations and was normal in 73% of the cases with cardiac manifestations.

Table 15: ECG in relation to Cardiac Manifestations in study Groups

STUDYGROUP	ECG	Cardiac Manifestations		Total	(%)	Sig
		With	Without			
CASES	Abnormal	8	0	8	16%	<0.01
	Normal	3	39	42	84%	
	Total	**11**	**39**	**50**	**100%**	
CONTROL	Abnormal	1	0	1	2%	
	Normal	1	48	49	98%	>0.05
	Total	**2**	**48**	**50**	**100%**	

Chart 13: **ECG in relation to Cardiac Manifestations in study Groups**

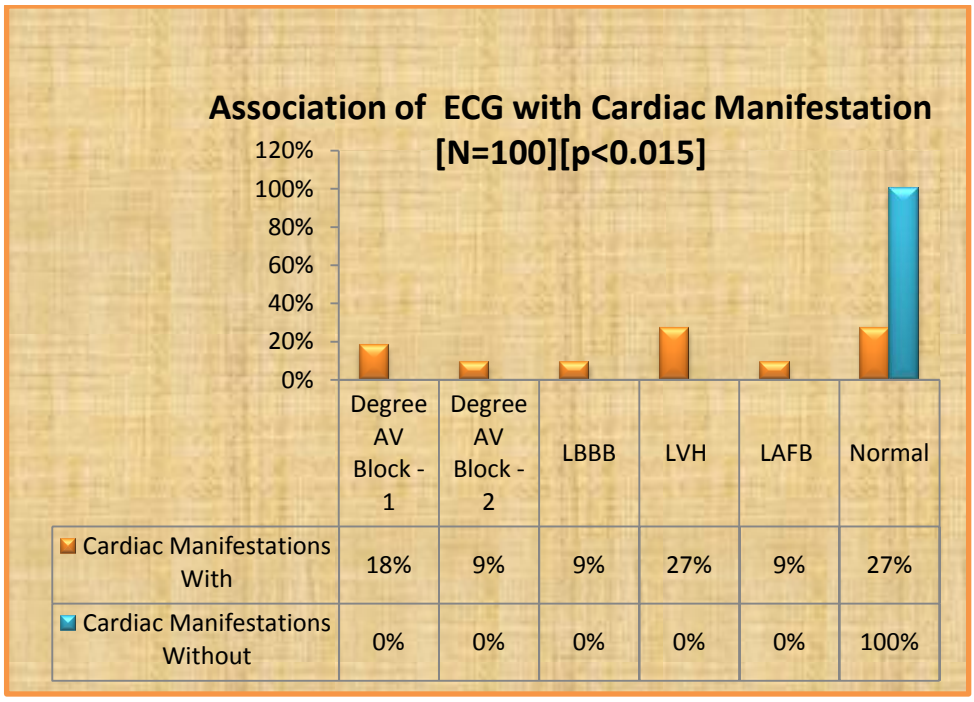


ECG was found to be abnormal in 8 out of 11 cases (73%) and normal in 3 out of 11 cases (27%) with cardiac manifestations whereas it was abnormal in 1 out of 2 controls with the cardiac manifestations which was statistically highly significant (P<0.01).

Table 16: ECG abnormalities in cases with cardiac manifestations

	Cardiac Manifestations				
ECG	**With**	**Without**	**Total**	**(%)**	**Sig**
Degree AV Block - 1	2	0	2	4%	
Degree AV Block - 2	1	0	1	2%	
LBBB	1	0	1	2%	
LVH	3	0	3	6%	<0.01
LAFB	1	0	1	2%	
Normal	3	39	42	84%	
Total	**11**	**39**	**50**	**100%**	

Chart 14: ECG abnormalities in cases with cardiac manifestations



ECG among the cases with cardiac manifestations showed conduction disturbances (45%) and left ventricular hypertrophy (27%) and normal(27%). The conduction disturbances noted were first and second degree Atrio-ventricular block, left anterior fascicular block, left bundle branch block.

Table 17: ECG abnormalities in cases and controls with cardiac manifestations

STUDYGROUP	ECG	Cardiac Manifestations		Total	(%)	Sig
		With	Without			
CASES	Degree AV Block - 1	2	0	2	4%	
	Degree AV Block - 2	1	0	1	2%	
	LBBB	1	0	1	2%	
	LVH	3	0	3	6%	<0.01
	LAFB	1	0	1	2%	
	Normal	3	39	42	84%	
	Total	**11**	**39**	**50**	**100%**	
CONTROL	LAFB	1	0	1	2%	
	Normal	1	48	49	98%	>0.05
	Total	**2**	**48**	**50**	**100%**	

Various ECG changes among the cases with cardiac manifestations was compared with that among the controls which was statistically significant shown in the table above and the chart below.

Chart 15: ECG abnormalities in cases and controls with cardiac manifestations

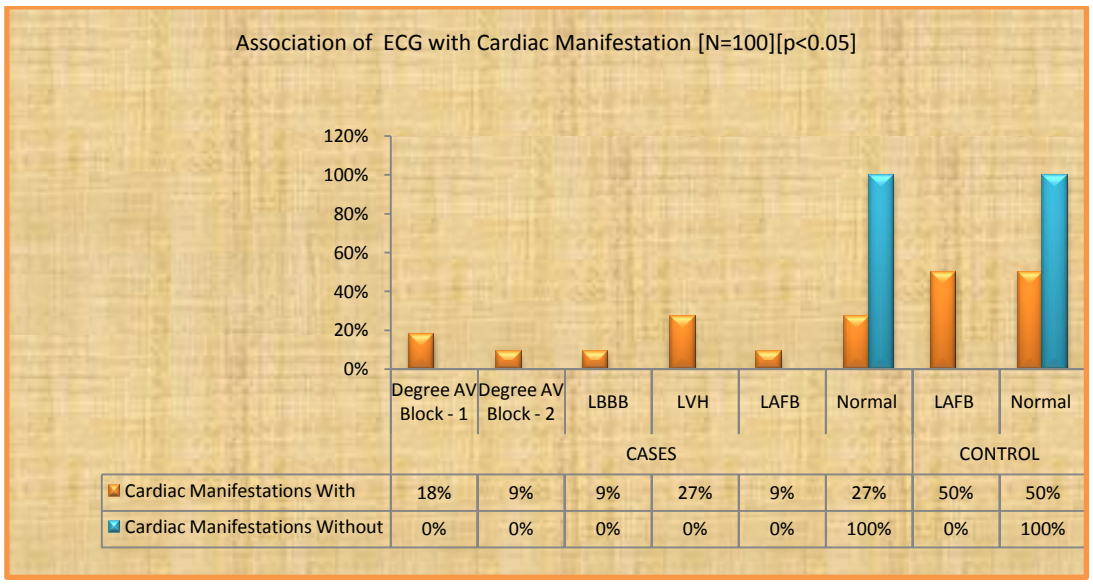
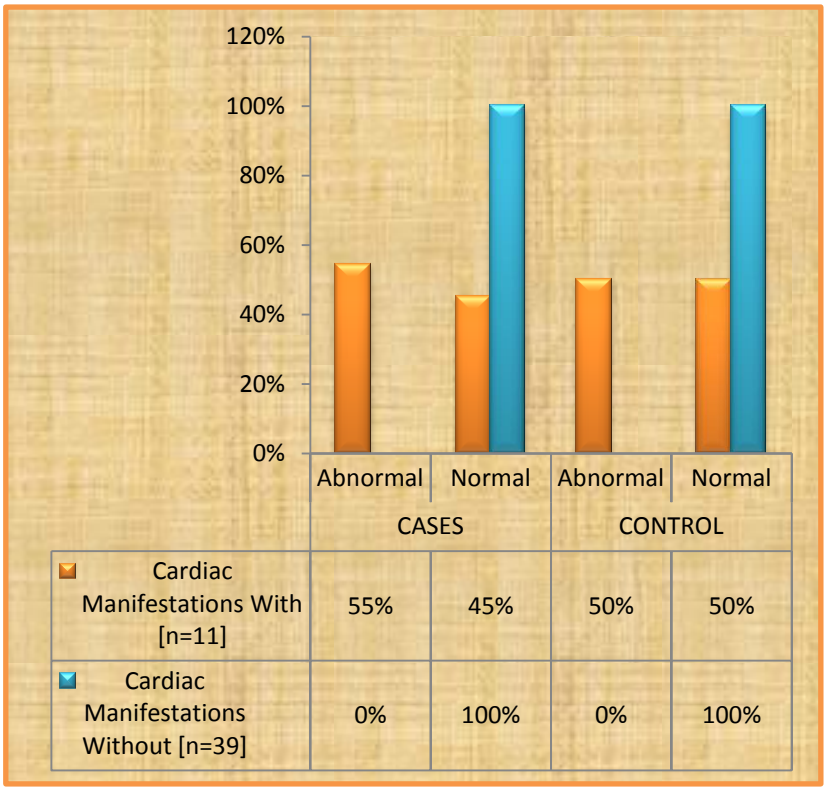


Table 18: ECHO in relation to Cardiac Manifestations in study Groups

STUDYGROUP	ECHO	Cardiac Manifestations		Total	(%)	Sig
		With	Without			
CASES	Abnormal	6	0	6	12%	<0.01
	Normal	5	39	44	88%	
	Total	**11**	**39**	**50**	**100%**	
CONTROL	Abnormal	1	0	1	2%	
	Normal	1	48	49	98%	>0.05
	Total	**2**	**48**	**50**	**100%**	

Chart 16: ECHO in relation to Cardiac Manifestations in study Groups

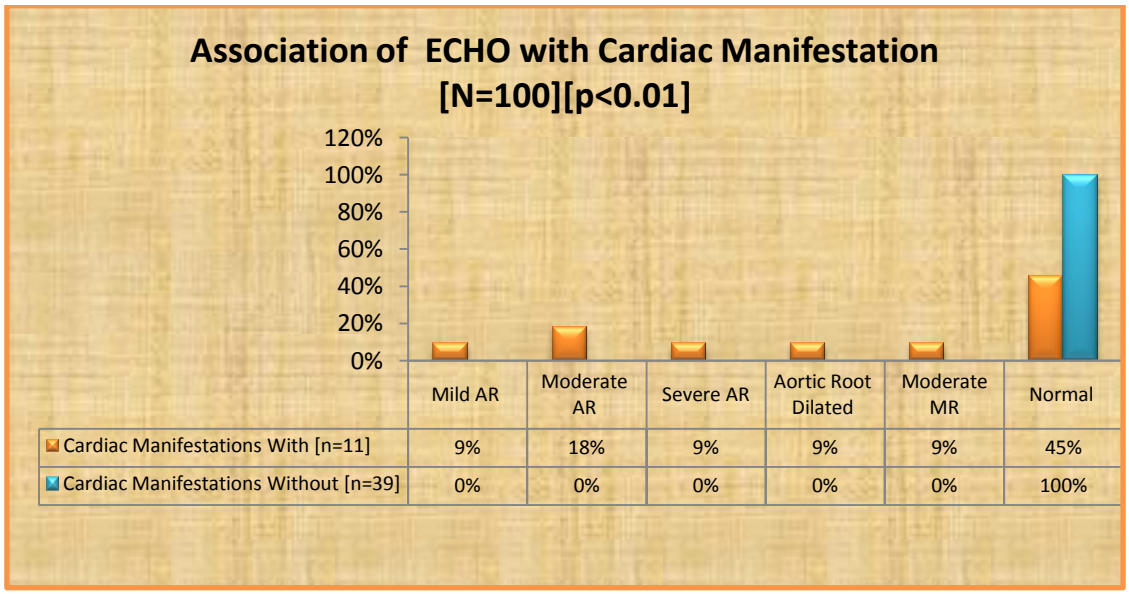


Echocardiographic was found to be abnormal in 6 out of 11 cases (55%) and normal in 5 out of 11 cases (45%) with cardiac manifestations whereas it was abnormal in 1 out of 2 controls with the cardiac manifestations. The association was statistically highly significant ($P<0.01$) .

Table 19: Echocardiographic abnormalities in cases with Cardiac Manifestations

ECHO	Cardiac Manifestations		Total	(%)	Sig
	With	Without			
Mild AR	1	0	1	2%	
Moderate AR	2	0	2	4%	
Severe AR	1	0	1	2%	
Aortic Root Dilated	1	0	1	2%	<0.01
Moderate MR	1	0	1	2%	
Normal	5	39	44	88%	
Total	**11**	**39**	**50**	**100%**	

Chart 17: Echocardiographic abnormalities in cases with Cardiac Manifestations

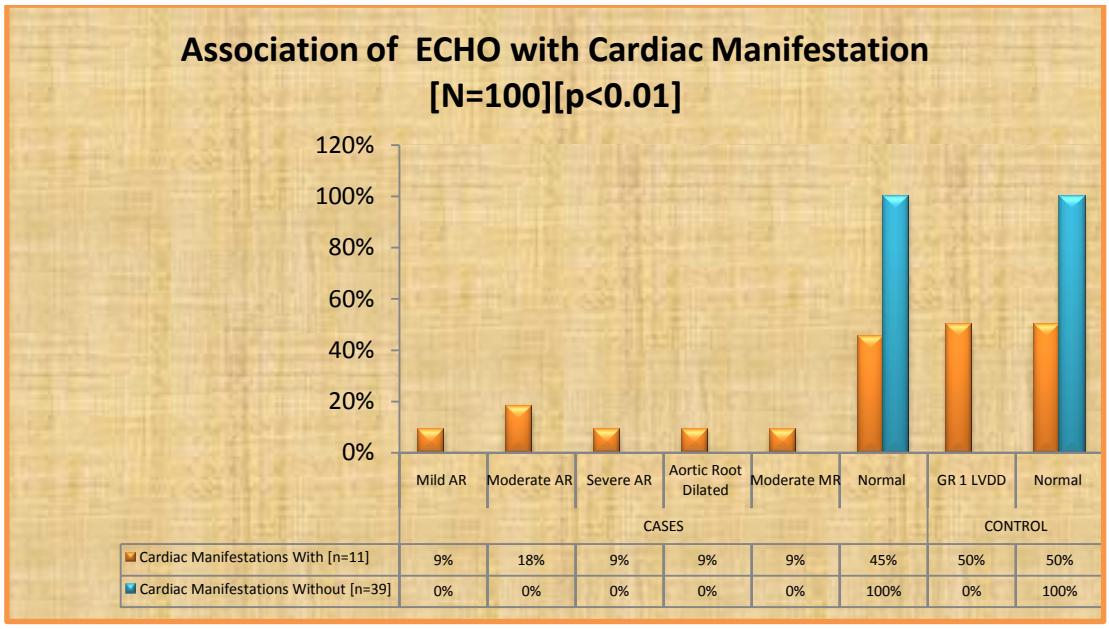


Echocardiographic findings among the cases with cardiac manifestations showed Aortic regurgitation (36%) and Isolated Aortic root dilatation (9%) and Mitral regurgitation (9%). Aortic regurgitation was mild in 9%, moderate in 18%, severe in 9% among the cases with cardiac manifestations. Aortic root dilatation was associated with aortic regurgitation in 2 of the cases.

Table 20: Echocardiographic abnormalities in cases and controls with Cardiac Manifestations

STUDYGROUP	Echo	Cardiac Manifestations		Total	(%)	Sig
		With	Without			
CASES	Mild AR	1	0	1	2%	
	Moderate AR	2	0	2	4%	
	Severe AR	1	0	1	2%	
	Aortic Root Dilated	1	0	1	2%	<0.01
	Moderate MR	1	0	1	2%	
	Normal	5	39	44	88%	
	Total	**11**	**39**	**50**	**100%**	
CONTROL	GR 1 LVDD	1	0	1	2%	
	Normal	1	48	48	96%	>0.05
	Total	**2**	**48**	**50**	**100%**	

Chart 18: Echocardiographic abnormalities in cases and controls with Cardiac Manifestations



Various Echocardiographic changes among the cases with cardiac manifestations was compared with that among the controls which was statistically significant. ($P<0.05$).

Table 21:Mean Clinical Variables in cases in relation to cardiac mmanifestations

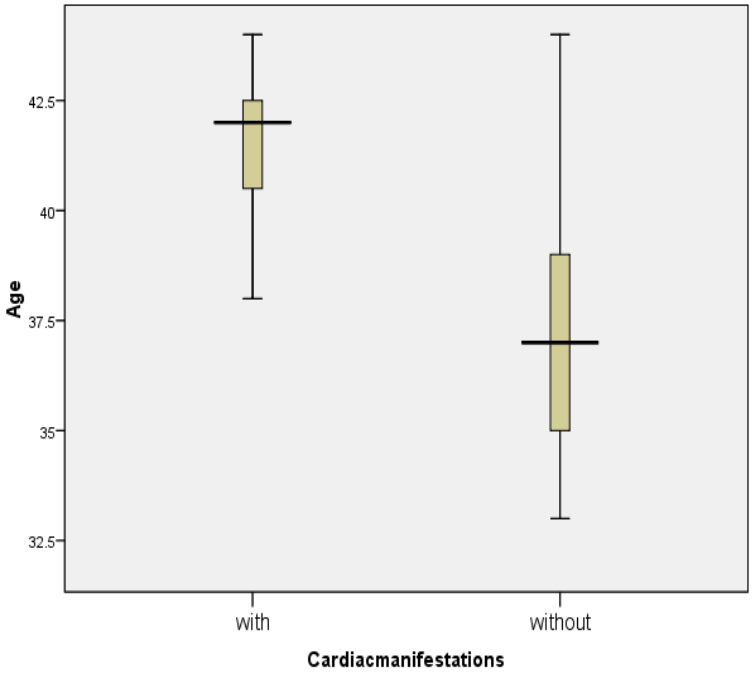
	Cardiac Manifestation	Mean	SD	95% CI for Mean		Minimum	Maximum	Sig
				Lower	Upper			
Age	WITH	41.45	1.695	40.32	42.59	38	44	
	WITHOUT	37.15	2.749	36.26	38.04	33	44	<0.001
	Total	38.1	3.112	37.22	38.98	33	44	
Duration	WITH	8.36	1.502	7.35	9.37	6	11	
	WITHOUT	4.33	1.675	3.79	4.88	1	8	<0.001
	Total	5.22	2.341	4.55	5.89	1	11	
CRP	WITH	13.36	5.784	9.48	17.25	8	28	
	WITHOUT	16.72	6.836	14.5	18.93	5	30	>0.05
	Total	15.98	6.711	14.07	17.89	5	30	

Mean of clinical variables

Age	41+/-1.7	37+/-2.7	<0.001
Duration of Disease	8.4+/-1.5	4.3+/-1.7	<0.001
CRP [mg/dl]	13.4+/-5.8	16.7+/-6.8	>0.05

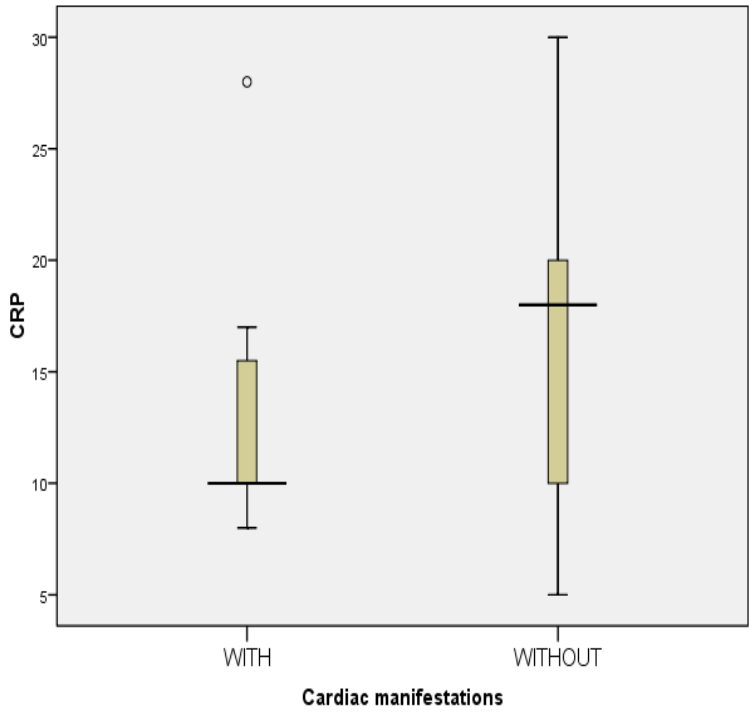
This table shows mean clinical variables – age of the cases, duration of the disease, CRP among the cases with and without cardiac manifestations and their statistical significance. Age and duration of the disease is statistically significant whereas CRP is not significant statistically in relation to cases with and without cardiac manifestations.

Chart 19: Mean age in cases with and without cardiac manifestations



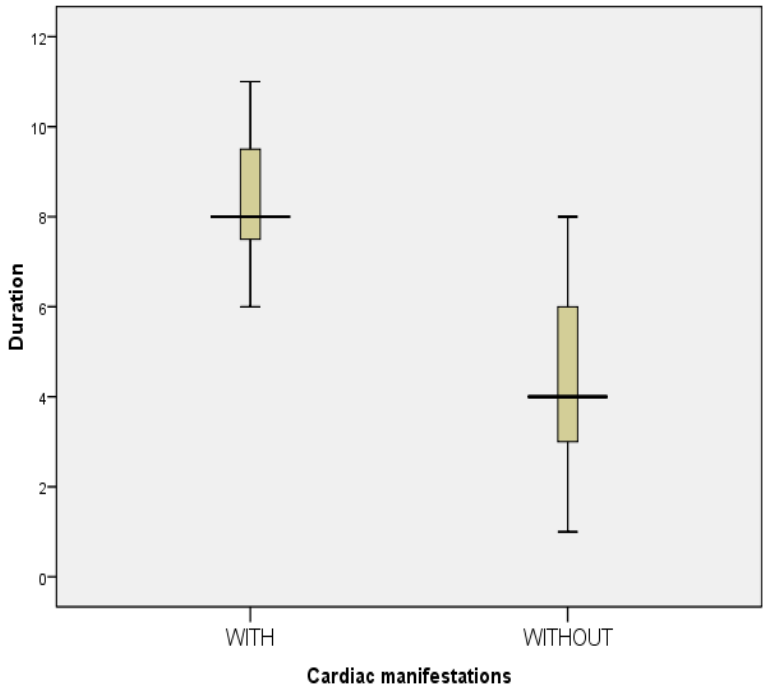
This box plot chart shows that the mean age of the cases with cardiac manifestations is 41.45 with a standard deviation (SD) of 1.695 (40.32 to 42.59) and range from 38 to 44 years and those without cardiac manifestations with mean of 37.15, SD of 2.749 (36.26 to 38.04) and range from 33 to 44 years. This shows statistical significance of P< 0.001

Chart 20: Mean CRP value in cases with and without cardiac manifestations



This box plot chart shows that the CRP of the cases with cardiac manifestations has a mean value of 13.36 with a standard deviation (SD) of 5.784 (9.48 to 17.25) and range from 8 to 28 mg/dl and those without cardiac manifestations shows a mean of 16.72, SD of 6.836 (14.5 to 18.93) and range from 5 to 30 mg/dl. This association is not statistically significant (P>0.05).

Chart 21: Mean duration of cases with and without cardiac manifestations



This box plot chart shows that the mean duration of the cases with cardiac manifestations is 8.36 years with a standard deviation (SD) of 1.502 (7.35 to 9.37) and range from 6 to 11 years and those without cardiac manifestations has a mean of 4.33, SD of 1.675(3.79 to 4.88) and range from 1 to 8 years. This shows statistical significance of $P< 0.05$

SUMMARY DATA

Table 22: Association of clinical variables with Cardiac Manifestation in cases and their statistical significance

	Cardiac Manifestations		
	With [n=11]	Without [n=39]	
Age			
31- 35	0%	31%	
36 – 40	27%	56%	<0.05
41 -45	73%	13%	
Gender			
Male	82%	77%	
Female	18%	23%	>0.05
Duration of Disease(AS) in years			
0- 3 yrs	0%	31%	
4-6 yrs	9%	62%	<0.001
7-11 yrs	91%	8%	
No.of positive clinical parameters			
2	9%	33%	
3	82%	46%	>0.05
4	9%	21%	
Grading of AS by X Ray imaging			
2 B/L	9%	26%	
3 U/L	36%	44%	
3 B/L	27%	10%	>0.05
4 U/L	18%	18%	
4 B/L	9%	3%	
ECG			
Degree AV Block – 1	18%	0%	
Degree AV Block – 2	9%	0%	
LBBB	9%	0%	<0.01
LVH	27%	0%	
LAFB	9%	0%	
Normal	27%	100%	
ECHO			
Mild AR	9%	0%	
Moderate AR	18%	0%	
Severe AR	9%	0%	
Aortic Root Dilated	9%	0%	<0.01
Moderate MR	9%	0%	
Normal	45%	100%	

Thus when cases with and without cardiac manifestations were compared, a significant statistical correlation was found with Age, Duration of the disease, ECG findings and Echocardiography and not so with Sex, Number of positive clinical parameters present in relation to the disease, Grading of sacroiliitis in AS by X Ray imaging.

Table 23:ECG and ECHO abnormalities in cases and controls and their statistical significance

	STUDY GROUP		
	CASES [n=50]	CONTROL [n=50]	
ECG			
Abnormal	16%	2%	
Normal	84%	98%	<0.05
ECHO			
Abnormal	12%	2%	
Normal	88%	98%	<0.05

The association is statistically significant when the ECG and Echocardiographic findings are compared among the cases and controls.

DISCUSSION

DISCUSSION:

Cardiac involvement is a well documented extraarticular manifestation among the patients suffering from ankylosing spondylitis. These abnormalities have been documented in several studies using echocardiography, electrocardiography.

In this study cardiac conduction abnormalities and valvular abnormalities were seen in 11 patients with ankylosing spondylitis. Among them cardiac conduction abnormalities were seen in 5 (10%), aortic regurgitation in 4(8%), Isolated aortic root dilatation(2%), mitral regurgitation(2%). Cardiac conduction abnormalities seen were first degree heart block (4%), second degree heart block (2%), left anterior fascicular block(2%), left bundle branch block(2%). Aortic regurgitation was mild in 2%, moderate in 4%, severe in 2%. 4% of AR were associated with aortic root dilatation.

Age and sex distribution:

The mean age of patients with ankylosing spondylitis was 38.1 years and that of the controls was 38.3 years. The age of the patients in the study group ranged from 31 – 45 years. The maximum prevalence of cardiac manifestations was between 41 – 45 years among the cases. Mean age of cases with cardiac manifestations was 41.45 years. Asociation of age of the cases with and without cardiac manifestations is statistically significant ($P<0.05$)

The study has 50 cases and 50 controls among which 39 are male cases and 11 are female cases and 35 are male controls with 15 of female controls. The male to female ratio in the cases was 3.5:1, in which cadiac manifestations occurred in 9 male caases and 2 female cases. Cardiac abnormalities occurred in 2 male controls.

S.Sukenik et al, [35] made a study with 40 patients with a mean age of the cases being 44.6 years, with 37 male cases and 3 female cases. The mean age of these patients was slightly higher than in our study.

Duration of Ankylosing Spondylitis:

In this study there were significantly higher prevalence of cardiac involvement in patients with increased duration of ankylosing spondylitis.The duration of the disease in the cases varied from 1 – 11 years. Higher prevalence of cardiac manifestations occurred between the duration of 7 – 11 years(91%). The mean duration of disease in patients with cardiovascular manifestations was 8.36 years. This had statistiscally significant correlation when compared with patients with and without cardiac manifestations ($P<0.001$).

O,Neill.T.W.et al, [34]conducted study in twenty four patients with a disease duration of more than or equal to ten years and found cardiac abnormalities in 29% of the cases.

Roldan et al, [36] conducted a study on cardiovascular manifestations in cases suffering from ankylosing spondylitis and found that the association was increased with increased duration of the disease.

Number of positive clinical parameters, severity of ankylosing spondylitis by X Ray grading, C- Reactive protein, all these parameters had no significant correlation with the occurrence of cardiac manifestations in patients with ankylosing spondylitis (P>0.05)

Roldan et al, [36] in the study had described that cardiac manifestations in patients with ankylosing spondylitis was unrelated to the disease activity, severity.

Electrocardiogram:

In the study, 16% of the cases had electrocardiographic changes among which 10% had conduction abnormalities in the form of first degree heart block, second degree heart block, left bundle branch block and left anterior fascicular block. 6% of the cases had left ventricular hypertrophy according to Romhilt Estes criteria. 2% of the controls had left anterior fascicular block. The association of electrocardiographic manifestations in the cases with and without cardiac manifestations was statistically significant (P<0.01) and also that between the cases and controls (P<0.05)

Helena Forsblad-d'Eliaet al, [37] in the study found that 10-33% of patients with ankylosing spondylitis had conduction disturbances , mostly of first degree atrioventricular block, complete bundle branch blocks.

S.Sukenik et al, [35] in the study conducted in forty patients found out that eight patients(20%), had conduction disturbances in the form of atrioventricular block and bundle branch block.

O, Neill et al, [34] in the study conducted in twenty four patients with ankylosing spondylitis found that significant 10% of the cases had conduction abnormalities.

Echocardiogram:

In the study 12% of the cases were with echocardiographic abnormalities among which 8% of the patients had aortic regurgitation, 2% had mitral regurgitation, 2% had isolated aortic root dilatation and 4% aortic regurgitation was associated with aortic root dilatation. This had statistically significant association in the cases with and without cardiac manifestations($P<0.01$) and that between the cases and the controls($P<0.05$).

O.Neill T.W. et al, [34] in the study of twenty four patients found that two patients had aortic regurgitation(8%).

Several studies had found the prevalence of aortic regurgitation to be high in patients with ankylosing spondylitis when the patients are subjected to trans oesophageal echocardiography rather than transthoracic echocardiography and also early valvular changes have been found with transoesophageal echocardiography, as done by Roldan et al.[36]

The prevalence of cardiovascular abnormalities in the present study would have been higher if transesophageal echocardiography has been done and if the duration of ankylosing spondylitis in the cases had been longer.

CONCLUSION

CONCLUSION:

- Cardiovascular manifestations in ankylosing spondylitis were seen in 11 out of 50 cases. Maximum prevalence occurred in the age group of 41-45 years with a male to female ratio of 3.5:1.Mean age of the cases with cardiovascular abnormalities was found to be 41.45 years.
- Duration of ankylosing spondylitis among the cases in the study group varied between 1 – 11 years. The maximum prevalence of Cardiovascular manifestations in AS occurred in patients with increased duration of the disease. Mean duration of the diease associated with cardiovascular manifestations was found to be 8.36 years.
- No significant correlation was found in association with sex, increased number of positive clinical parameters to the occurrence of cardiovascular manifestations in ankylosing spondylitis.
- Increase in C-Reactive protein, grading of sacroiliitis by X Ray, cardiac symptoms in AS, Chest X Ray also were not found to be significantly associated with the cardiovascular manifestations.
- Three patients had cardiomegaly (6%) in the chest X Ray and those patients had cardiac symptoms like chest pain and breathlessness.
- The electrocardiogram revealed significant cardiac conduction abnormalities (10%) and left ventricular hypertrophy(6%) among the cases. Conduction abnormalities were first degree AV block (4%), second degree AV block(2%), left anterior fascicular fascicular

block(2%), left bundle branch block (2%) whereas only 2% of control subjects had conduction abnormalities in ECG, left anterior fascicular block.

- The echocardiographic abnormalities were found in 12% of the cases which had significant association in patients with AS. Most common abnormality found among AS patients were aortic regurgitation (8%) [Mild – 2%, Moderate – 4%, severe – 2%]. One case had moderate mitral regurgitation (2%) and one another had aortic root dilatation(2%) with 4% aortic regurgitation associated with aortic root dilatation.

SUMMARY

SUMMARY:

The study was conducted in 50 cases, the patients suffering from ankylosing spondylitis who had attended the outpatient and Inpatient departments at the Coimbatore medical college hospital and 50 controls who were selected on a random basis. The association of cardiovascular manifestations with the disease were found among the cases and various factors of the disease influencing the manifestations were studied and they were compared with the control group.

- Cardiovascular abnormalities are important extraarticular manifestations in patients with ankylosing spondylitis. These abnormalities can be clinical or sub clinical.
- When patients with ankylosing spondylitis were evaluated, 11(22%) out of 50 patients had some form of cardiovascular abnormalities.Out of this 10% had conduction abnormalities in electrocardiogram and 10% had valvular regurgitation, 2% had isolated aortic root dilatation by echogardiography. Among these 4% of aortic regurgitation was associated with aortic root dilatation.
- Most common was aortic regurgitation among the valvular diseases(8%), other was mitral regurgitation and Isolated aortic root dilatation. Common conduction disturbance was first degree AV block.
- The maximum prevalence of cardiac abnormalities were found between the age group of 41-45 years indicating that as the age goes on, the

prevalence of cardiac manifestations increase. Male to female ratio of 3.5:1 with more incidence among the males.

- High prevalence of cardiac involvement occurred in patients with increased duration of the disease ranging from 7 – 11 years with a mean duration of disease being 8.36 years.
- Statistically significant association of the cardiovascular manifestations occurred with increase in the age, duration of the disease.
- No significant association was found with the gender, increase in the number of positive clinical parameters of the disease, increase in C-Reactive Protein, grading of sacroiliitis by X Ray imaging, CXR, Cardiac symptoms in ankylosing spondylitis.
- Thus the conduction disturbances in electrocardiography and valvular lesions and aortic root dilatation in echocardiography among the cases were statistically significant when compared with the controls.
- Since cardiovascular abnormalities are one of the most common cause of mortality in patients with ankylosing spondylitis, these should be detected early and thereby it will assess in the proper management of the patients with the disease at the appropriate time.
- Therefore it is mandatory that every patient with ankylosing spondylitis should undergo cardiac evaluation to help in early detection and treatment of cardiovascular abnormalities, to reduce the morbidity and mortality associated with the disease and to improve the quality of life of patients with ankylosing spondylitis.

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ANNEXURES

PROFORMA:

NAME: AGE/SEX: OP/IP NO:

ADDRESS:

HISTORY:

ANKYLOSING SPONDYLITIS:

ARTICULAR SYMPTOMS:

Duration of back pain:

Duration of morning stiffness:

Number of extra axial joints involved:

EXTRAARTICULAR SYMPTOMS:

Malaise, fatigue, low grade fever

Cough, Chest pain

Dyspnoea, giddiness

Swelling of legs

Ocular symptoms

Skin lesions

Muscle weakness

Bladder and bowel habits

FAMILY HISTORY OF ANKYLOSING SPONDYLITIS:

TREATMENT HISTORY:

Pain relief with response to NSAIDs and treatment with other drugs.

PHYSICAL EXAMINATION:

GENERAL EXAMINATION:

Pulse: Blood pressure:

Pallor/clubbing/cyanosis

Pedal oedema/icterus/lymphadenopathy

Ocular and dermatological examination

SYSTEMIC EXAMINATION:

CARDIOVASCULAR:

JVP

Inspection Palpation

Percussion Auscultation

Respiratory

Abdominal

Neurological

RHEUMATOLOGICAL

Axial joints involved

Extra axial joints involved

Joint deformities

INVESTIGATIONS:

Haemoglobin: WBC count:

Platelet count: ESR: CRP:

X – Ray B/L Sacro iliac joints

X-Ray of involved axial and peripheral joints

Chest X-Ray

12 LEAD ELECTROCARDIOGRAM

ECHOCARDIOGRAM:

Cardiac Position: Pericardium:

Great vessels: IAS and IVS:

Cardiac chambers:

Right atrium: Left atrium:

Right Ventricle: Left ventricle:

Valves (velocities across the valves and grading of regurgitations as described earlier in methodology)

Mitral Aortic

Pulmonary Tricuspid

Aortic Root Diameter:

Left Ventricular Internal diastolic Diameter:

Left Ventricular Internal Systolic Diameter:

EF%: E/A:

CONSENT FORM

Mr/Mrs/Ms……

…….(relationship) of……(legal guardian) is being asked to be a participant in the research study titled

"STUDY OF CARDIOVASCULAR MANIFESTATIONS IN ANKYLOSING SPONDYLITIS" in CMC Hospital, Coimbatore, conducted by **Dr.BARATHI.L,** Post Graduate Student in the Department of General Medicine, Coimbatore Medical College. He /she satisfies eligibility as per the inclusion criteria. You/legal guardian can ask any question you may have before agreeing to participate.

Research Being Done

STUDY OF CARDIOVASCULAR MANIFESTATIONS IN ANKYLOSING SPONDYLITIS

Purpose of Research

Aim of the study is to find out the incidence of cardiovascular manifestations in ankylosing spondylitis

Procedures involved

. It includes details like age, sex, history of axial and peripheral joint involvement, cardiac symptoms and other extraarticular symptoms, treatment history and family history as well as clinical examination.

Investigations includes complete hemogram, ESR, CRP, X Ray bilateral sacroiliac joints and involved peripheral joints, Chest X-Ray, Electrocardiogram and Echocardiogram.

Decline from Participation

You have the option to decline from participation in the study existing protocol for your condition.

Privacy and Confidentiality

Privacy of individuals will be respected and any information about you or provided by you during the study will be kept strictly confidential.

Authorization to publish Results

Results of the study may be published for scientific purposes and/or presented to scientific groups, however you will not be identified.

STATEMENT OF CONSENT

I volunteer and consent to participate in this study. I have read the consent or it has been read to me. The study has been fully explained to me, and I may ask questions at any time.

---------- ----------

Signature /Left thumb impression Date

(volunteer)

---------- ----------

Signature of witness Date

ஒப்புதல் படிவம்

பெயர் .

வயது .

பாலினம் .

முகவரி .

அரசு கோவை மருத்துவக் கல்லூரியில் பொது மருத்துவ துறையில் பட்ட மேற்படிப்பு பயிலும் மாணவி **மரு.ல.பாரதி** அவர்கள் மேற்கொள்ளும் **"ஆன்கைலோஸிங் ஸ்பான்டைலைட்டிஸ் நோயின் இருதய வெளிப்பாடுகள் பற்றிய ஆய்வு"** என்பதின் செய்முறை மற்றும் அனைத்து விளக்கங்களையும் கேட்டுக் கொண்டு எனது சந்தேகங்களை தெளிவுப்படுத்திக் கொண்டேன் என்பதை தெரிவித்துக் கொள்கிறேன்.

நான் இந்த ஆய்வில் முழு சம்மதத்துடனும், சுய சிந்தனையுடனும் கலந்து கொள்ள சம்மதிக்கிறேன்.

இந்த அய்வில் என்னைப் பற்றிய அனைத்து விவரங்கள் பாதுகாக்கப்படுவதுடன் இதன் முடிவுகள் ஆய்விதழில் வெளியிடப்படுவதில் ஆட்சேபனை இல்லை என்பதை தெரிவித்துக் கொள்கிறேன். எந்த நேரத்திலும் இந்த ஆய்வில் இருந்து நான் விலகிக் கொள்ள எனக்கு உரிமை உண்டு என்பதையும் அறிவேன்.

இடம்

தேதி கையொப்பம் / ரேகை

MASTER CHART

KEY TO MASTER CHART

Sl.No	:	Serial number
OP/IP NO	:	Outpatient/Inpatient number
Sex	:	M – Male, F – Female
Dis.dura	:	Duration of AS in years
Clin.Para	:	Number of positive clinical parameters in AS (ASAS Criteria)
CRP	:	C Reactive Protein in mg/dl
Grading	:	Grading of sacroiliitis in AS by X Ray
B/L	:	Bilateral
U/L	:	Unilateral
N	:	Normal
Symptom	:	Cardiac symptoms
C.megaly	:	Cardiomegaly
CXR	:	Chest X Ray
ECG	:	Electrocardiogram
Echo	:	Echocardiogram
E/A	:	Peak Early (E) / Late (A) trans mitral filling velocities (N – 0.75 to 1.5)
EF	:	Ejection Fraction

A.Root.D	:	Aortic root diameter (N- 2.5 to 4)
Card.M	:	Cardiac manifestations
1 D AV Bl	:	First degree atrioventricular block
2 D AV Bl	:	Second degree atrioventricular block
LBBB	:	Left bundle branch block
LAFB	:	Left anterior fascicular block
LVH	:	Left ventricular hypertrophy
LVDD	:	Left ventricular diastolic dysfunction
A.R.Dil	:	Aortic root dilation
Mild AR	:	Mild Aortic regurgitation
Mod AR	:	Moderate Aortic regurgitation
SevAR	:	Severe Aortic regurgitation
Mod MR	:	Moderate Mitral regurgitation

MASTER CHART CASES

Sl.No	Name	OP/IP NO	Age	Sex	Dis.Dura	Clin.para	CRP	Grading	Symptom	CXR	ECG	E/A	EF%	A.Root.D	Echo	Card.M
1	S.Sahayaraj	16096	38	M	8	3	10	2 - B/L	Nil	N	1 D AV Bl.	0.95	64	3.6	N	Yes
2	N.Siva	114483	41	M	7	3	20	3 - U/L	Nil	N	N	1.15	67	3.2	N	No
3	D.Palanisamy	583543	36	M	3	2	8	2 - B/L	Nil	N	N	1.2	68	3.4	N	No
4	S.Bagyalakshmi	710297	39	F	4	3	11	4 - U/L	Nil	N	N	1.5	65	2.8	N	No
5	L.Nanjappan	862017	40	M	6	4	26	3 - U/L	Nil	N	N	1.34	64	2.8	N	No
6	G.Krishnaswamy	95222	42	M	8	3	10	3 - U/L	Nil	N	N	1.45	69	4.2	A.R.Dil.	Yes
7	N.Maheshwari	622607	41	F	5	3	20	4 - U/L	Nil	N	N	1.25	70	3.1	N	No
8	G.Nandhakumar	843556	35	M	3	2	16	3 - U/L	Nil	N	N	1.35	67	3.4	N	No
9	V.Manikandan	1527	33	M	2	2	12	2 - B/L	Nil	N	N	1.43	65	3.6	N	No
10	B.Suresh	68356	34	M	2	2	9	3 - U/L	Nil	N	N	1.24	64	3.5	N	No
11	L.Jeyaraj	211099	37	M	5	3	18	2 - B/L	Nil	N	N	1.45	67	3.1	N	No
12	S.Sharmila	178978	34	F	4	2	8	3 - U/L	Nil	N	N	1	64	2.6	N	No
13	N.Ramasamy	58479	44	M	10	4	28	3 -U/L	Dyspnoea	C.megaly	LVH	0.8	54	3.9	Mod AR	Yes
14	A.Musthaffa	800616	42	M	7	3	14	4 - U/L	Nil	N	N	1	63	2.9	Mod MR	Yes
15	T.Dhanapal	128177	33	M	2	2	16	3 - U/L	Nil	N	N	1.14	67	3.5	N	No
16	V.Shankar	233702	42	M	6	4	23	3 - B/L	Nil	N	N	1.24	67	3.7	N	No
17	G.Veeramani	191443	36	F	5	3	26	2 - B/L	Nil	N	N	1.12	68	3.6	N	No
18	R.Selvaraj	853671	38	M	6	2	9	3 - B/L	Nil	N	N	1.1	69	2.9	N	No
19	S.Chinnapparaj	74207	37	M	5	2	10	4 -U/L	Nil	N	N	1.25	70	3.1	N	No
20	N.Gurumoorthy	51873	36	M	3	3	19	3 - B/L	Nil	N	N	1.34	68	3.2	N	No
21	J.Kalaivani	61284	34	F	4	3	30	3 - U/L	Nil	N	N	1.18	65	3.4	N	No
22	M.Marimuthu	139266	40	M	6	4	24	2 -B/L	Nil	N	N	1.46	67	3.2	N	No
23	J.Stephenraj	65285	43	M	10	3	14	3 = U/L	C.Pain	C.megaly	LVH	0.7	51	4.6	Mod AR	Yes
24	D.Sivaprakasam	21829	36	M	5	3	25	3 - U/L	Nil	N	N	1.36	67	2.8	N	No
25	M.Yogeshwaran	57864	37	M	6	2	5	4 - U/L	Nil	N	N	1.21	68	2.7	N	No
26	M.Samsath	577695	40	F	9	3	10	3 - B/L	Nil	N	2 D AV Bl	0.85	69	2.6	N	Yes
27	L.Deivamani	7856	34	M	2	4	8	3 - U/L	Nil	N	N	1.38	72	3.5	N	No

MASTER CHART CASES

Sl.No.	Name	OP/IP No.	Age	Sex	Dis.Dura	Clin.para	CRP	Grading	Symptom	CXR	ECG	E/A	EP%	A.Root.D	Echo	Card.M
28	N.Duraisamy	198263	38	M	6	3	19	4 - U/L	Nil	N	N	1,16	65	3.6	N	No
29	S.Nagarathnam	6479	36	M	4	3	11	2 -B/L	Nil	N	N	1,42	68	2.8	N	No
30	B.Ragamathulla	2898	35	M	2	3	18	3 - U/L	Nil	N	N	1.41	66	2.8	N	No
31	K.Srinivasan	61243	40	M	7	3	9	4 - B/L	Nil	N	N	1.15	65	3.4	N	No
32	V.Ramesh	30625	41	M	8	3	9	4 - U/L	Nil	N	LBBB	1.4	67	3.6	N	Yes
33	K.Jothi	44482	39	F	4	2	13	3 - U/L	Nil	N	N	1.39	69	3.7	N	No
34	M.Damodarasamy	4317	41	M	5	3	20	2 - B/L	Nil	N	N	1.16	68	3.8	N	No
35	S.Jeyaraman	58944	37	M	2	3	18	3 - U/L	Nil	N	N	1.43	65	3.6	N	No
36	M.Kalimuthu	54872	38	M	4	4	30	3 - U/L	Nil	N	N	1.5	64	2.8	N	No
37	M.Shanthi	432149	34	F	1	3	20	2 - B/L	Nil	N	N	1.27	65	2.9	N	No
38	N.Arumugam	284729	35	M	3	2	9	3 - U/L	Nil	N	N	0.9	69	3.6	N	No
39	B.Gowri	46565	41	F	6	3	17	3 - U/L	Nil	N	N	1.14	67	3.5	Mild AR	Yes
40	M.Krishnaraj	167922	44	M	8	4	16	2 - B/L	Nil	N	N	1.29	69	3.2	N	No
41	S.Sivakumar	25951	43	M	8	2	8	4 - B/L	Nil	N	1 D AV Bl.	1.18	70	3.4	N	Yes
42	N.Gopalakrishnan	51369	40	M	6	3	24	3 - B/L	Nil	N	N	1.38	69	3.9	N	No
43	R.Natarajan	61248	38	M	5	2	10	2 -B/L	Nil	N	N	1.26	65	3.4	N	No
44	S.Jothimani	43078	38	F	4	4	27	4 - U/L	Nil	N	N	1.43	71	2.8	N	No
45	M.Abbas	2542	40	M	7	3	17	3 - B/L	Nil	N	LAFB	1.17	68	2.9	N	Yes
46	M.Senthil kumar	53387	36	M	3	3	20	3 - U/L	Nil	N	N	1.28	65	2.7	N	No
47	R.Manikandan	61794	39	M	6	4	19	4 - U/L	Nil	N	N	1.5	67	2.8	N	No
48	L.Murugan	6572	34	M	4	3	17	3 - U/L	Nil	N	N	1.42	68	3.6	N	No
49	V.Usha	193259	34	F	4	2	9	3 - U/L	Nil	N	N	1.03	69	3.4	N	No
50	D.Jayaraman	63274	42	M	11	3	10	3 - B/L	Dyspnoea	C.megaly	LVH	0.6	46	4.8	Sev AR	Yes

MASTER CHART CONTROLS

Sl.No.	Name	OP. NO	Age	Sex	CRP	Symptom	CXR	ECG	E/A	EF%	A.Root.D	Echo	Card.M
1	V.Sathish kumar	12568	32	M	6	Nil	N	N	1.25	70	2.8	N	No
2	G.Mallika	45896	33	F	7	Nil	N	N	1.2	67	3.1	N	No
3	K.Prabakaran	21825	35	M	4	Nil	N	N	1.4	68	3.1	N	No
4	B.Deivanai	23671	41	F	3	Nil	N	N	1.03	68	3.4	N	No
5	D.Logeshwaran	8754	44	M	7	Nil	N	N	1.16	65	3.2	N	No
6	N.Mani	67690	38	M	6	Nil	N	N	1.45	67	3.3	N	No
7	R.Mariammal	56675	34	F	2	Nil	N	N	0.95	68	2.8	N	No
8	S.Pichaimuthu	45872	40	M	3	Nil	N	N	1.03	70	2.8	N	No
9	M.Gnanavel	453179	44	M	5	Nil	N	N	1.01	65	3.4	N	No
10	B.Vasudevan	156687	45	M	11	Nil	N	N	1.37	68	3.5	N	No
11	L.Yeshodha	23485	34	F	5	Nil	N	N	1.45	67	2.7	N	No
12	C.Baskaran	46572	33	M	6	Nil	N	N	1.3	64	2.7	N	No
13	N.Arogyaraj	56778	42	M	4	Nil	N	N	1.15	67	2.6	N	No
14	V.Jeyabalan	22435	36	M	4	Nil	N	N	1.4	69	2.8	N	No
15	S.Muthulakshmi	54712	38	F	3	Nil	N	N	1.35	66	2.9	N	No
16	A.Nagaraj	6469	38	M	5	Nil	N	N	0.88	68	3.1	N	No
17	V.Eswari	53245	39	F	6	Nil	N	N	1.4	67	3.2	N	No
18	A.Shahul hameed	56698	34	M	2	Nil	N	N	1.05	68	3.1	N	No
19	S.Gopalraj	36557	44	M	4	Nil	N	N	1.15	64	2.8	N	No
20	K.Balamurugan	98769	45	M	5	Nil	N	LAFB	1.2	65	2.6	N	Yes
21	M.Krishnaraj	87690	37	M	6	Nil	N	N	1.33	70	2.7	N	No
22	L.Sathyamoorthy	67453	41	M	14	Nil	N	N	1	68	3.1	N	No
23	N.Ponnammal	435617	42	F	5	Nil	N	N	1.2	67	3.4	N	No
24	J.Muthusamy	66687	36	M	6	Nil	N	N	1.41	68	3.5	N	No
25	N.Peter	78634	35	M	5	Nil	N	N	1.34	69	3.2	N	No
26	S.Karuppuraj	871235	44	M	5	Nil	N	N	1.35	64	2.6	N	No
27	A.Kadheeja	25487	41	F	8	Nil	N	N	1.21	70	2.7	N	No
28	R.Eshwaran	5980	34	M	9	Nil	N	N	1.25	68	2.8	N	No
29	P.Senthil	67553	32	M	4	Nil	N	N	1.41	65	2.6	N	No

MASTER CHART CONTROLS

Sl.No.	Name	OP. NO	Age	Sex	CRP	Symptom	CXR	ECG	E/A	EF%	A.Root.D	Echo	Card.M
30	K.Manjula	45987	39	F	3	Nil	N	N	1.2	65	3.1	N	No
31	D.Sethupathi	167436	41	M	3	Nil	N	N	1.31	67	3.2	N	No
32	N.Manickaraj	76534	44	M	2	Nil	N	N	1.15	68	3.2	N	No
33	D.Vasantha	98675	38	F	2	Nil	N	N	1.5	67	2.6	N	No
34	G.Yogaraj	125627	39	M	4	Nil	N	N	1.23	69	2.7	N	No
35	N.Chinnaraj	56987	40	M	10	Nil	N	N	1.44	67	2.7	N	No
36	S.Latha	212560	35	F	5	Nil	N	N	0.95	70	2.6	N	No
37	M.Pandian	64576	40	M	4	Nil	N	N	1.12	68	3.1	N	No
38	N.Rani	56547	38	F	5	Nil	N	N	1.15	66	3.1	N	No
39	G.Ponnusamy	65930	43	M	5	Nil	N	N	0.85	71	2.8	N	No
40	A.Mohammed kadar	56873	41	M	7	Nil	N	N	1.4	69	2.8	N	No
41	S.Kavitha	64578	33	F	8	Nil	N	N	1.3	68	2.7	N	No
42	B.Muthupandi	352479	34	M	5	Nil	N	N	1.26	67	3.1	N	No
43	G.Manickavel	45879	41	M	6	Nil	N	N	1.43	68	3.4	N	No
44	C.Baskaran	65794	38	M	6	Nil	N	N	1.35	65	2.8	N	No
45	N.Manju	44758	36	F	7	Nil	N	N	0.92	67	2.6	N	No
46	K.Kalaiarasan	45698	40	M	8	Nil	N	N	1.28	67	2.8	N	No
47	N.Selvaraj	4593	39	M	8	Nil	N	N	1.3	69	2.7	1 LVDD	Yes
48	D.Suresh	24956	32	M	5	Nil	N	N	0.9	65	2.6	N	No
49	R.Kalarani	76925	40	F	7	Nil	N	N	1.12	68	3.1	N	No
50	N.Kathikeyan	67942	34	M	8	Nil	N	N	1.2	69	2.8	N	No

MASTER CHART - CASES WITH CARDIAC MANIFESTATIONS

Sl.No	Name	OP/IP NO	Age	Sex	Dis.Dura	Clin.para	CRP	Grading	Symptom	CXR	ECG	E/A	EF%	A.Root.D	Echo
1	S.Sahayaraj	16096	38	M	8	3	10	2 - B/L	Nil	N	1 D AV Bl.	0.95	64	3.6	N
2	G.Krishnaswamy	95222	42	M	8	3	10	3 - U/L	Nil	N	N	1.45	69	4.2	A.R.Dil.
3	N.Ramasamy	58479	44	M	10	4	28	3 -U/L	Dyspnoea	C.megaly	LVH	0.8	54	3.9	Mod AR
4	A.Musthaffa	800616	42	M	7	3	14	4 - U/L	Nil	N	N	1	63	2.9	Mod MR
5	J.Stephenraj	65285	43	M	10	3	14	3 = U/L	C.Pain	C.megaly	LVH	0.7	51	4.6	Mod AR A.R.Dil.
6	M.Samsath	577695	40	F	9	3	10	3 - B/L	Nil	N	2 D AV Bl	0.85	69	2.6	N
7	V.Ramesh	30625	41	M	8	3	9	4 - U/L	Nil	N	LBBB	1.4	67	3.6	N
8	B.Gowri	46565	41	F	6	3	17	3 - U/L	Nil	N	N	1.14	67	3.5	Mild AR
9	S.Sivakumar	25951	43	M	8	2	8	4 - B/L	Nil	N	1 D AV Bl.	1.18	70	3.4	N
10	M.Abbas	2542	40	M	7	3	17	3 - B/L	Nil	N	LAFB	1.17	68	2.9	N
11	D.Jayaraman	63274	42	M	11	3	10	3 - B/L	Dyspnoea	C.megaly	LVH	0.6	46	4.8	Sev AR A.R.Dil.